CORLAS 2025

August 25 - 27 | Stockholm, Sweden

Annual Meeting

Swedish Society of Medicine

Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum

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CORLAS 2025
Stockholm, Sweden

Dear CORLAS Members,

We are delighted to invite you to the CORLAS 2025 (Collegium Oto-Rhino-Laryngologi-cum Amicitiae Sacrum) Annual Meeting, to be held in central Stockholm, Sweden, at the art nouveau-style Swedish Society of Medicine, from Monday, August 25 to Wednesday, August 27, 2025.

Since its founding in 1926 CORLAS has become an annual international academic gathering point for physicians and researchers in the field of oto-rhino-laryngology and head and neck surgery. Our members are internationally recognized for their outstanding achievements in research and clinical development. Traditionally our annual meetings are alternating between the different continents. The meeting not only provides numerous opportunities for academic exchange but in its warm atmosphere also establishes friendly relationships among the members.

In addition to the academic sessions, we are pleased to announce that the traditional family excursion will take place by boat, exploring the Stockholm Archipelago. Following the conference, we will also offer a post-conference tour to the island of Gotland, where you can experience its natural beauty and rich cultural heritage from the iron age and medieval times.

CORLAS remains committed to promoting peace and cultural understanding by encouraging friendship and cooperation between ENT colleagues across the world. In these times of increasing unrest, this mission is more vital than ever, and we believe that the bonds of fellowship we build strengthen both our profession and the global community.

We and the Nordic CORLAS members invite you and your distinguished colleagues to join the CORLAS 2025 congress in Stockholm and welcoming you with a spirit of cordial hospitality.

Warmly Welcome

Lars Olaf Cardell, President
Matti Anniko, Vice President

CORLAS Board at the 2025 Stockholm Meeting

Board

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1926 H. Zwaardemaker Groningen / The Netherlands (founding meeting)
1927 F.R. Nager Zurich / Switzerland
1928 F. Schmiegelow Copenhagen / Denmark (business meeting)
1929 A.A. Gray London / Great Britain
1930 C. Voss Frankfurt am Main / Germany
1931 G. Portmann Bordeaux / France
1932 A.G. Tapia Madrid / Spain (business meeting)
1933 A. Precechtel Prague / Czech Republic
1934 G. Holmgren Stockholm / Sweden
1935 A. Rejto Budapest / Hungary
1937 F. Brunetti Venice / Italy
1938 A. de Kleyn Groningen / The Netherlands
1947 C. Hicquet Brussels / Belgium (informal meeting)
1948 N.Rh. Blegvad Copenhagen / Denmark (informal meeting)
1949 N.Rh. Blegvad London / Great Britain (business meeting)
1950 G. Ferreri Rome / Italy (informal meeting)
1951 Y. Meurman Helsinki / Finland (business meeting)
1952 L. Ruedi Zurich / Switzerland
1953 L. Ruedi Amsterdam / T. Netherlands (business meeting)
1954 V.E. Negus London / Great Britain
1955 B. Gusic Zagreb-Belgrade / Yugoslavia
1956 G. Portmann Bordeaux / France
1957 G. Portmann Washington / USA (business meeting)
1958 G.T. Wilson Dublin / Ireland
1959 G. Hofer Vienna / Austria
1960 M. Arslan Padua / Italy
1961 M. Arslan Paris / France (business meeting)
1962 J. Chryssikos Athen / Greece
1963 I. Simson Hall Edinburgh / Great Britain
1964 H. Wullstein Würzburg / Germany
1965 H. Wullstein Tokyo / Japan (business meeting)
1966 P. Mounier-Kuhn Lyon / France
1967 J. Lindsay Chicago / USA
1968 T. Leegard Oslo / Norway
1969 T. Leegard Mexico City / Mexico (business meeting)
1970 E. Borghesan Palermo / Italy
1971 W.H. Struben Rotterdam / The Netherlands
1972 E. Escher Berne / Switzerland
1973 E. Escher Venice / Italy (business meeting)

Presidents cont'd

1974 J. Angell James Bristol / Great Britain
1975 I.F. Padovan Dubrovnik / Croatia
1976 C.A. Hamberger Stockholm / Sweden
1977 C.A. Hamberger Buenos Aires / Argentina (business meeting)
1978 M. Ciges Granada / Spain
1979 L. Surjan Budapest / Hungary
1980 F.A. Sooy San Francisco / USA
1981 F.A. Sooy Budapest / Hungary (lunch meeting)
1982 L.B.W. Jongkees The Hague / The Netherlands
1983 P. Pialoux Paris / France
1984 L.S. Manolidis Corfu / Greece
1985 A. Coyas Miami / USA (lunch meeting)
1986 H.H. Naumann Munich / Germany
1987 G. Rossi Turin / Italy
1988 I. Watanabe Tokyo / Japan
1989 I. Watanabe Madrid / Spain (lunch meeting)
1990 C.R. Pfaltz Basel / Switzerland
1991 D.F.N. Harrison York / Great Britain
1992 M.N. Kotby Cairo / Egypt
1993 M.N. Kotby Istanbul / Turkey (lunch meeting)
1994 M. Andrea Estoril / Portugal
1995 K. Albegger Salzburg / Austria
1996 P.W. Alberti Vancouver / Canada
1997 P.W. Alberti Sydney / Australia (lunch meeting)
1998 P. Bretlau Copenhagen / Denmark
1999 A. Morgan Lyon / France
2000 J.B. Snow Washington / USA
2001 J.B. Snow postponed
2002 P. van den Broek Noordwijk / The Netherlands, Cairo / Egypt (lunch meeting)
2003 R. Grénman Helsinki / Finland
2004 P. Mangabeira Albernaz Salvador / Brazil
2005 P. Mangabeira Rome / Italy (lunch meeting)
2006 G. Tavartkiladze Moscow / Russia
2007 C.S. Kim Seoul / Korea
2008 H. Scherer Berlin / Germany
2009 H. Scherer Sao Paolo / Brazil (lunch meeting)
2010 I. Sziklai Budapest / Hungary
2011 P. Lefebvre Bruges / Belgium
2012 R. Filipo Rome / Italy

Presidents cont'd

2013 M. Önerci Seoul / Korea (lunch meeting)
2014 M. Önerci Istanbul / Turkey
2015 P.A. Wackym San Francisco / USA
2016 R. Dauman Bordeaux / France
2017 O. Sterkers Paris / France (lunch meeting)
2018 W.N. Huang Beijing / China
2019 M. Kompis Berne / Switzerland
2020 M. Goycoolea / Pandemic – Virtual business meeting
2021 M. Goycoolea / Pandemic – Virtual business meeting and virtual presentations
2022 M. Goycoolea Santiago / Chile
2023 T. Yamasoba Tokyo / Japan
2024 W-D. Baumgartner Vienna / Austria
2025 L-O Cardell Stockholm / Sweden

General Secretaries

1926 – 1940 C.E. Benjamins Groningen
1940 – 1960 E. Huizinga Groningen
1960 – 1976 L.B.W. Jongkees Amsterdam
1977 – 1986 C.R. Pfaltz Basel
1987 – 2000 P. van den Broek Nijmegen
2000 – 2008 P. Karma Helsinki
2008 – 2015 R. Dauman Bordeaux
Since 2015 A. Mäkitie Helsinki

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1926 – 1936 A.R. Tweedie Nottingham
1936 – 1950 V.E. Negus London
1950 – 1966 L. Ruedi Zurich
1966 – 1990 M. Portmann Bordeaux
1990 – 1999 J.M. Aran Bordeaux
2000 – 2008 R. Dauman Bordeaux
2008 – 2015 R. Grénman Turku
Since 2016 S. Stöckli St. Gallen

Congress Information

Venue

Swedish Society of Medicine
Klara Östra Kyrkogata 10
101 35 Stockholm

The Swedish Society of Medicine's building was constructed between 1904 and 1906 and is considered one of the most important pioneering works of National Romanticism in Sweden. We offer unique conference facilities, located in the heart of Stockholm.

Welcome to Stockholm

Welcome to the capital of Sweden, a vibrant and picturesque city built on 14 islands where Lake Mälaren meets the Baltic Sea. With a unique blend of medieval heritage and modern innovation, Stockholm offers visitors a rich cultural experience in a clean, safe, and walkable environment.

In August, the city is at its best – with long daylight hours, mild temperatures, and a lively atmosphere. Stroll through the cobbled streets of the Old Town (Gamla Stan), visit world-renowned museums like the Vasa Museum or Fotografiska, and enjoy the many parks, waterfront cafés, and scenic views.

Getting around is easy thanks to an efficient public transportation system that includes metro, buses, trams, and ferries – all accessible with a single ticket. Arlanda International Airport is located just 40 minutes from the city center.

We hope you take the opportunity to enjoy both the congress and the many experiences that Stockholm has to offer.

Congress Information

Language

The official language of the congress is English.

Opening Hours

Sunday August 24 12.00 – 15.00
Monday August 25 07.00 – 17.30
Tuesday August 26 07.30 – 17.30
Wednesday August 27 07.30 – 15.30

Exhibition Opening Hours

Monday August 25 10.00 – 15.30
Tuesday August 26 09.30 – 16.00
Wednesday August 27 09.00 – 14.00

Name Badges

You will receive a personalized badge upon registration. This badge must be clearly visible at all times during the Congress and grants access to the Scientific Sessions and the Exhibition. Please also wear it at all social events to be identified as a participant of CORLAS 2025.

Certificate of Attendance

An Attendance Certificate will be sent by email to all officially registered participants after the congress.

Offical CORLAS Group Photo

The official group photo will be taken at the City Hall August 26.
Before the reception begins, all members will gather outside City Hall for a photo at 18:45.

Lunch and Coffee Breaks

Members and guests participating in the scientific programme will have lunch and fika at Svenska Läkaresällskapet (Swedish Society of Medicine).
Accompanying persons will have lunch and afternoon fika at Hotel At Six.
Lunch will be served at 12:00 and afternoon coffee at 15:00.

Congress Information

Information for Oral Presentation

To ensure a smooth and professional experience during your session, please note the following important information regarding your presentation:

- A dedicated presentation computer will be available in the lecture hall. To avoid technical issues, we kindly recommend that you do not use your own laptop.

- A technician will be present in the hall and assist you when it is time for your presentation.

- Presentations should be prepared in PowerPoint format (16:9 aspect ratio).

- We kindly ask you to submit your presentation well in advance.
Deliver your presentation to the technician in Room ”Ordföranderummet, no later than 2 hours before your session starts.

- The technician will check that your presentation runs correctly on the presentation computer.

Thank you for participation!

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Sincere thanks are extended to the Swedish Society for Otorhinolaryngology, Head and Neck Surgery for their kind support and endorsement of the conference.

Social Program

Morning run with the professors

We are pleased to announce that the professors will lead a morning run Tuesday Aug 26 at 06.45 AM.
Departing from Hotel At Six, Brunkebergstorg 6.
All participants are welcome to join this invigorating start to the day.

Dinners

Welcome reception at Sällskapet 24/8

We are pleased to invite you and your families to a welcome buffet at Sällskapet, one of Sweden's oldest and most distinguished gentlemen's clubs. Since 1870, Sällskapet has been a gathering place for tradition and camaraderie, with H.M. King Carl XVI Gustaf as its first honorary member.

The evening will take place in the club's historic premises at Arsenalsgatan 7, offering an elegant and exclusive setting for good company and conversation.

Sällskapet maintains a formal dress code

Men: A jacket, tailored trousers, and a tie or bowtie are required.
Women: Should dress in an equally formal and elegant manner, in line with the dress code for men.
Children: Should also be appropriately dressed.
Not permitted (for both men and women): Jeans, sneakers and boots (regardless of color or fabric).

Etiquette

- Mobile phones may not be used within the premises.
- Photography is strictly prohibited inside the club.

Please adhere to these guidelines to respect the club's traditions and atmosphere.

Details

Venue: Sällskapet
Address: Arsenalsgatan 7
Date: Sunday 24/8
Time: 19.00
Costs: Included in your registration fee
Participant Registration & Badge Collection: Registration for participants, where you can collect your name badge, will open at 18.15.

Dinners

Member's Dinner at Posthuset 25/8

We are delighted to invite you to a members´ evening at Posthuset!

Located at Vasagatan 28, Posthuset is a historic landmark, originally built between 1903 and 1906 in a grand neo-Renaissance style to serve as Stockholm's main post office. Posthuset is an architectural masterpiece, blending monumental proportions with intricate details that reflect Sweden's early 20th-century elegance. Today, this beautifully restored building provides a unique setting where history meets modern refinement.

Join us for a memorable gathering, featuring great company, a delightful three-course dinner, and carefully selected beverages in this stunning and historic venue. The evening offers a perfect opportunity to unwind, connect with fellow CORLAS members, and experience a piece of Stockholm's architectural heritage in an inviting and elegant atmosphere.
Members and guests will have dinner in "Orangeriet", while accompanying persons will have dinner in "Palmsalen".

Do not forget your CORLAS tie!

Details
Venue: Posthuset – Orangeriet and Palmsalen
Address: Vasagatan 28
Date: Monday 25/8
Time: 19.00
Costs: Included in your registration fee

Dinners

Cultural Evening at Stockholm City Hall 26/8

We are honored to invite you to a reception at Stockholm City Hall!
This magnificent venue is where the prestigious Nobel Prize Banquet is held each year in the presence of the Swedish Royal Family, the Nobel Prize Committee, and all Nobel Laureates with their guests.

Hosted by Stockholm City and Region Stockholm, this evening celebrates CORLAS and offers a unique opportunity to experience one of Sweden's most iconic landmarks. We will then enjoy a buffet dinner and an exclusive guided tour of City Hall, providing insight into its rich history and stunning architecture.

Important information
Visitors and guests to events may bring bags no larger than 21x30 cm (A4 size) into the premises. Bags and other items that exceeds these measurements must be stored in the staffed cloakrooms. Visitors and guests may have their bags and other items searched before being granted access to the premises.

Details
Venue: Stockholm City Hall
Address: Hantverkargatan 1
Date: Tuesday 26/8
Time: 19.00 (Please arrive on time as speeches will begin promptly.)
Costs: Included in your registration fee
Dress code: Business casual

Dinners

Gala Dinner at Operaterassen 27/8

We are delighted to invite you to a Gala Dinner at Operaterrassen!
Located within the prestigious Operakällaren, this iconic venue offers breathtaking views of Stockholm Palace, providing a refined and elegant setting for this special evening.

Join us for an evening where you will enjoy world-class cuisine in one of Stockholm's most renowned establishments. This event is a highlight of the CORLAS gathering, offering the perfect opportunity to connect with fellow members, engage in meaningful conversations, and celebrate in a setting of sophistication and tradition.

To honor the formal nature of the evening, we kindly suggest Black Tie (full tuxedo) for gentlemen, and elegant evening wear for ladies.

Details

Venue: Operakällaren – Operaterrassen
Adress: Karl XII:s torg 1
Date: Wednesday 27/8
Time: 19.00
Costs: Included in your registration fee

Family Tour 24/8

Join us for an unforgettable pre-meeting excursion through Stockholm's archipelago on Sunday, August 24. This tour, designed exclusively for us, offers a good opportunity to reconnect with colleagues and their families, make new friends.
We will embark on a historic journey aboard M/S Gustafsberg VII, a beautifully preserved 1912 vessel that combines old-world charm with modern comfort. As we glide past thousands of idyllic islands, rugged coastlines, and picturesque seaside villages, you will have a lunch with classic Nordic flavors and then later, Swedish Fika with freshly brewed coffee and traditional baked treats.

This day tour offers a good opportunity to experience the Stockholm archipelago in the company of old and new friends.
Further details and registration information will be shared soon. We look forward to welcoming you aboard!

Price per Person: SEK 1540 excl VAT (SEK 1925 incl VAT)

Departure: Sunday August 24 at 11.00
Return: Sunday August 24 at 15.00
Departure & Return Location: Strandvägen, Berth 15, Stockholm

Included in the Tour
Two-course lunch
Starter: Three kinds of herring, spiced cheese, chives, sour cream
Main course: Swedish meatballs, potatoes, brown sauce, lingonberries, and pressed cucumber
Afternoon coffee & pastries: Around 14.00, coffee/tea with cinnamon buns

Post-Congress Tour to Gotland 28-30/8

Join us for an exclusive post-conference tour to Gotland, specially arranged for CORLAS participants. Experience a rich blend of history, nature, and culture as we journey together from Stockholm to the UNESCO-listed Hanseatic town of Visby.

We'll travel by bus to Nynäshamn and then by ferry to Visby, with lunch served en route. In Visby, we'll stay two nights at the historic Wisby Börs Hotel, reserved exclusively for our group.

Tour Highlights

- Guided tour through Visby's medieval streets, ruins, and city walls
- Cycling tour beyond Visby, exploring Gotland's countryside, Iron Age sites, and coastal landmarks
- Culinary experiences showcasing regional specialties
- Optional participation in traditional medieval sports

We return to Stockholm on Saturday evening, with time to catch late or next-day flights.

This unique trip offers a chance to reconnect with colleagues and explore Gotland in the relaxed spirit of CORLAS.

About Gotland

Gotland, Sweden's largest island, is entirely surrounded by the Baltic Sea, shaping its striking and diverse landscape. It boasts dramatic limestone cliffs, rugged sea stacks (rauks), and vast coastal meadows. The island's porous bedrock creates a unique, dry environment, home to sparse pine forests and vibrant wildflower fields. With Viking history, unique nature, and local delicacies, Gotland offers a perfect mix of culture and relaxation.

Post-Congress Tour to Gotland 28-30/8

Thursday August 28

09.00: Bus transfer from the conference hotel Stockholm to Nynäshamn ferry terminal
11.25: Ferry departs for Visby (lunch included)
15.00: Arrival in Visby, transfer to Wisby Börs Hotel, and check-in
17.00: Activity Visby
19.00: Dinner at Restaurant Bolaget

Friday August 29

08.00: Morning jog with the professor
Morning: Breakfast
10.00: Activity Gotland including biking
16.00: Academic historic lecture
19.00: Rustic dinner in a medieval cellar

Saturday August 30

Morning: Breakfast
09.00: Activity Gotlandic pentathlon (lunch not included)
15.00: Transfer to ferry terminal
16.00: Ferry departs to Nynäshamn (dinner included)
19.25: Arrival in Nynäshamn, followed by a bus transfer, arriving at Stockholm Central around 20.45.
If you wish to leave earlier, there is a ferry departing from Visby at 07.15, which you will need to book on your own. After the ferry, you travel by train to Arlanda Airport, arriving around noon. The route is: Visby (Gotland) - Nynäshamn - Stockholm Central - Arlanda.

Price per Person

Double room per person (2 persons in the room): SEK 13 580 excl VAT, (SEK 16 975 ink VAT)
Single room per person (1 person in the room): SEK 15 580 excl VAT (SEK 19 475 ink VAT)

Price Includes

-Round-trip transfer from central Stockholm to Nynäshamn
-Round-trip ferry ticket with reserved seating, including lunch on the way to Gotland and dinner on the return
-Round-trip transfer from the ferry terminal to the hotel
-Two nights at Börs Hotel including breakfast
-Activity: "A grand tour of Visby"
-Activity: "A grand tour of Gotland beyond Visby," including lunch
-Activity: Gotlandic Pentathlon
-Three-course dinner at Restaurant Bolaget, including welcome drink and beverage package
-Rustic three-course dinner in a medieval cellar, including welcome drink and beverage package
-Medieval musician entertainment during dinner

City Tours

City Tours	Monday, August 25	Tuesday, August 26	Wednesday, August 27
Visit the Nobel Museum (14.00-15.00)	✔	✔	
Guided Tour of the Old Town in Stockholm (14.00-16.00)	✔	✔	✔
Guided Bus Tour of Stockholm with a Visit to the Vasa Museum (09.00-12.00)		✔	
Visit Skansen with Lunch (11.00-13.00)	✔		
Visit the ABBA Museum (10.00-11.30)		✔	✔
Visit Fotografiska with Lunch (10.00-13.00) CANCELLED			

Old Town

Discover the charm and history of Stockholm's enchanting Old Town (Gamla Stan) on a two-hour guided walking tour, starting and ending at Hotel At Six, Brunkebergstorg 6. Join us as we dive into the city's medieval heart, where cobblestone streets, colorful facades, and centuries-old stories await.

Walk through time as your guide brings legends to life, from the tales of Viking merchants to royal dramas within the walls of the Royal Palace. Discover Stortorget's iconic square, learn about the Nobel Prize's Stockholm roots, and experience the majesty of Stockholm Cathedral.

This tour is more than just history; it's an intimate look at Swedish culture, art, and architecture, all while taking in the unique atmosphere that defines Gamla Stan. Perfect for all ages, this two-hour experience is designed to fit into your day with ease, offering you the chance to see Stockholm from a whole new perspective.

Details

Time: 14.00-16.00
Date: 25, 26 or 27/8, you will have to choose one day
Costs: Included in your registration fee
Meeting Point: Hotel At Six, Brunkebergstorg 6

City Tours

Abba Museum

Join us for an unforgettable journey into the world of one of Sweden's greatest musical legends at the ABBA Museum in Stockholm! We'll gather outside Hotel At Six at 09.15 and travel together by subway to the museum, building up excitement for what awaits.

Once we arrive, an exclusive guided tour will take you through the fascinating history of ABBA, from their early days to global superstardom. Experience the band's iconic costumes, gold records, and original instruments. You'll even have the chance to step on stage and sing along with ABBA's holograms! Perfect for fans and newcomers alike, this visit promises music, memories, and a dash of Swedish pop magic.

Don't miss out on this extraordinary experience!

Details

Time: 10.00-11.30 (At Abba Museum, Djurgårdsvägen 68)
Date: 26 and 27/8
Costs: Included in the registration fee for Accompanying Person, 350 SEK for Guests and Members
Meeting Point: Hotel At Six, Brunkebergstorg 6. We meet at 09.15 to walk to the central station.

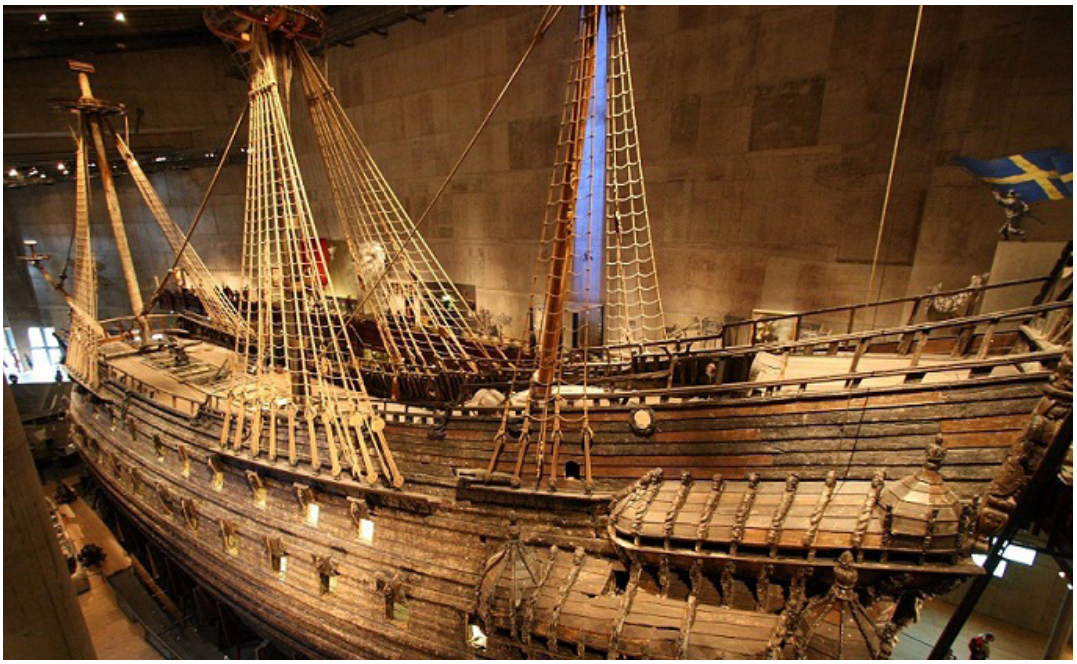
City Tours

Guided Bus Tour of Stockholm with a Visit to the Vasa Museum
Discover Stockholm's rich history and stunning landmarks on a guided bus tour through the Swedish capital. This comfortable and informative journey takes you past the city's most iconic sights, including the Royal Palace, the historic Old Town (Gamla Stan), and the picturesque waterfront areas.

A highlight of the tour is a visit to the world-famous Vasa Museum, home to the remarkably well-preserved 17th-century warship, the Vasa. Learn about the ship's fascinating history, its dramatic sinking in 1628, and the extensive efforts to restore it.

With an expert guide providing insights along the way, this tour offers a perfect mix of sightseeing and cultural exploration, making it an unforgettable experience in Stockholm.

Details
Time: 09.00-12.00
Date: 26/8
Costs: 650 SEK
Meeting Point: Hotel At Six, Brunkebergstorg 6



City Tours

Skansen with Lunch

Step back in time with "Sweden Through History" at Skansen, Stockholm's beloved open-air museum! We'll meet outside Hotel At Six at 10.15 and travel together by subway to Skansen, where a journey through Sweden's rich cultural heritage awaits.

Once there, experience Swedish history brought to life with authentic 19th-century homes, historic shops, traditional crafts, and lively reenactments. From rustic farmhouses to grand manor houses, Skansen offers an immersive experience of life as it was over the centuries, set against the stunning backdrop of Stockholm. We will end the tour with lunch at Gubbhyllan.

Our day will be filled with captivating stories, hands-on demonstrations, and insights into Swedish traditions. Perfect for history enthusiasts and those curious about Swedish culture, this tour will leave you with a deep appreciation for Sweden's past. Join us for a unique adventure and see history come alive at Skansen!

Details

Time: 11.00-13.00 (At Skansen, Djurgårdsslätten 49-51)
Date: 25/8
Costs: 650 SEK
Meeting Point: Hotel At Six, Brunkebergstorg 6. We meet at 10.15 to walk to the Central Station.

City Tours

Fotografiska with Lunch CANCELLED

Discover the magic of photography and visual art at Fotografiska in Stockholm, one of the world's premier museums dedicated to contemporary photography! We'll gather outside Hotel At Six and board a comfortable bus together to Fotografiska, where an inspiring day awaits. Our guided tour will take us through captivating exhibitions, offering deeper insights into the featured artists, their creative processes, and the thought-provoking themes explored through their lenses. After the tour, we'll relax over a delicious lunch at Fotografiska's restaurant.

Join us for a day filled with art, inspiration, and great company!

Details

Time: 10.00-13.00

Date: 26/8

Costs: 650 SEK

Meeting Point: Hotel At Six, Brunkebergstorg 6. A buss will pick you up and drive you to and from Fotografiska to Hotel At Six.

City Tours

Nobel Prize Museum

Join us for an unforgettable experience at the Nobel Prize Museum in Stockholm! We'll meet outside Hotel At Six at 13.30 and walk together to this iconic museum, where the legacy of the world's most prestigious award comes to life. Once inside, we'll embark on a guided tour through the Nobel Prize's fascinating history, discovering the incredible achievements of laureates across fields like physics, literature, and peace. Our expert guide will reveal the inspiring stories behind groundbreaking discoveries and the remarkable individuals who changed the world. Don't miss this chance to dive into the spirit of innovation, courage, and curiosity that defines the Nobel Prize!

Details

Time: 14.00-15.00 (At Nobel Prize Museum, Stortorget 2, it takes 20 minutes to walk from Hotel At Six)
Date: 25, 26/8
Costs: Included in the registration fee for Accompanying Person, 350 SEK for Guests and Members
Meeting Point: Hotel At Six, Brunkebergstorg 6

Scientific Programme Overview

Monday August 25

08.00-09.00	Opening Ceremony
09.10-10.00	Session 1 Ctrl+Alt+Research; AI takes the lead
10.00-10.15	**Coffee and mingle in the exhibition**
10.15-11.05	Session 2 Head and Neck Surgery 2.0: Nodes, Robots, and New Realities
11.10-12.30	Session 3 Big Ideas, Short Talks I
12.30-13.45	**Lunch**
13.45-15.10	Session 4 Symposium: CRS Reloaded – New Mechanisms, New Medicines, New Mindsets
15.10-15.25	**Coffee and mingle in the exhibition**
15.25-16.05	Session 5 Symposium: Rewiring Hearing: Gene Therapy and Inner Ear Innovation
16.10-17.10	General Assembly
19.00	**Members' Dinner (Posthuset – Orangeriet) Vasagatan 28** ***PS..Don't forget your CORLAS tie***

Tuesday August 26

08.00-09.30	Session 6 Big Ideas, Short Talks II
09.40-10.25	Session 7 The Edge of Innovation: Healing the Head and Neck
10.25-10.40	**Coffee and mingle in the exhibition**
10.40-11.45	Session 8 Big Ideas Short Talks III
11.50-12.45	Session 9 Big Ideas Short Talks IV
12.45-13.50	**Lunch**
13.50-14.45	Session 10 Unraveling Ear Disease: Genetic Drivers and Structural Defenses
14.50-15.30	Session 11 Otology
15.30-15.40	**Coffee and mingle in the exhibition**
15.40-17.05	Session 12 Symposium: CI in the Real World: Syndromes, Side Effects, and Cognitive Impact
19.00	**Cultural Evening at Stockholm City Hall, Hantverkargatan 1** *The City of Stockholm and the Stockholm Region are hosting the reception*

Wednesday August 27

08.00-09.00	Session 13 Silent Voices and Sleepless Nights: Rebuilding Airway Function
09.15-10.10	Session 14 Big Ideas, Short Talks V
10.10-10.25	**Coffee and mingle in the exhibition**
10.25-11.45	Session 15 Signals from the Labyrinth: Hearing and Balance in Focus
12.00-12.35	Session 16 Smell, Sight, and Survival: High-Stakes Rhinology
12.35-13.50	**Lunch**
13.50-15.10	Session 17 Vision for the Future from the CORLAS Experience
15.10-15.25	Closing ceremony
19.00	**Gala Dinner, Operakällaren – Operaterrassen, Karl XII:s torg 1**

Scientific Programme Details

MONDAY August 25th

8.00 – 9.00 Opening Ceremony
Lars Olaf Cardell, Congress President (Stockholm)
Antti Mäkitie, General Secretary (Helsinki)

Jay T Rubinstein (Seattle)
Introduction of the Shambaugh Prize Recipient

Keynote Lecture 1
Chair: Matti Anniko (Uppsala)
Thomas Perlman, Member of the Nobel Assembly, Karolinska Institutet and General Secretary of the Nobel Committee, Stockholm
The Nobel algorithm: truth, politics and the art of selection (25 min)

Keynote Lecture 2
Chair: Ann Hermansson (Lund)
Hans Herz, Professor in Biomedical Technology, Royal Institute of Technology, Stockholm
High-spatial-resolution laboratory x-ray imaging: towards next-generation pathology and radiology (25 min)

09.10 – 10.00 Session 1

Ctrl+Alt+Research; AI takes the lead
Chairs: Konstantina M. Stankovic (MEMBER, Palo Alto), Romain Kania (MEMBER, Paris)

S1 L1 Stephan Lang (MEMBER, Essen) Artificial Intelligence in Oto-Rhino-Laryngology: From Vision to Real-World Integration

S1 L2 Konstantina M. Stankovic (MEMBER, Palo Alto) Genetic Diagnosis and Discovery Enabled by Large Language Models

S1 L3 Kristina Simonyan (NEW MEMBER, Boston) From larynx to brain: AI-based diagnostics of neurological voice disorders

S1 L4 Paul Merkus (MEMBER, Amsterdam) CT-like images of the temporal bone from MRI using machine learning: development, validation and usefulness

S1 L5 Johan Frijns (MEMBER, Leiden) Better speech understanding and subjective experience with a novel artificial intelligence-based dereverberation algorithm in cochlear implant users

Discussion (10 min)

Fika (15 min)

10.15 – 11.05 Session 2

Head and Neck Surgery 2.0: Nodes, Robots, and New Realities
Chairs: Dale Brown (MEMBER, Toronto), Manuel Bernal-Sprekelsen (MEMBER, Barcelona)

S2 L1 Sandro Stoeckli (MEMBER, St Gallen) Long-term results of sentinel node biopsy for early oral and oropharyngeal squamous cell carcinoma

S2 L2 Linda Marklund (MEMBER, Uppsala) Sentinel node-assisted neck dissection in N+ oral squamous cell carcinoma

S2 L3 Hisham Mehanna (MEMBER, Birmingham) Accuracy and prognosis of extranodal extension on radiologic imaging in HPV+ oropharyngeal cancer: the multinational HNCIG-EPIC iENE study

S2 L4 Tobias Todsen (NEW MEMBER, Copenhagen) Surgeon-performed head and neck ultrasound in office-based and perioperative setting

S2 L5 Bevan Yueh (MEMBER, Minneapolis) Impact of Tumor Volume on Gastrostomy Use and Mortality in Advanced Laryngeal Cancer

S2 L6 Chia-Jung Busch (NEW MEMBER, Greifswald) First Experience with the DaVinci SP Robotic System in Germany: Opportunities and Challenges in Head and Neck Surgery

Pause (5 min)

11.10 – 12.30 Session 3

Big Ideas, Short Talks I
Miscellaneous (19 papers à 3 min and a poster)
Chair: Linda Marklund (MEMBER, Uppsala)

S3 L1 Pa-Chun Wang (MEMBER, Taipei) Competence-based Otolaryngology Resident Training – National Perspectives

S3 L2 Tessa Hadlock (MEMBER, Boston) Toward A Wearable Device for Facial Pacing

S3 L3 Chi-Te Wang (GUEST, New Taipei City) Bi-layered Microflap Technique for the Treatment of Anterior Glottic Web

S3 L4 Wei-Chung Hsu (MEMBER, Taipei) Ultrasonographic Changes of Upper Airway Structures in Children with Obstructive Sleep Apnea after Adenotonsillectomy

S3 L5 Uno Kosuke (GUEST, Tokorozawa) Transoral videolaryngoscopic surgery as a minimally invasive treatment for pyriform sinus fistula

S3 L6 Michael Tong (MEMBER, Hong Kong Sar) SmartHear+SmartTalk -AI empowering solutions for speech and hearing

S3 L7 Petri Olivius (MEMBER, Eskilstuna) An evaluation of an innovation and medical device for treatment of patients suffering from common outer ear and nose problems

S3 L8 Donna Martin (GUEST, Ann Arbor) Novel Chd7+/CreERT2 and Chd7FAST/+ mice for exploring cell lineage and overexpression as preclinical studies for gene therapy in CHARGE syndrome

S3 L9 Seong Keun Kwon (MEMBER, Seoul) Kink-Resistant and Flexible Scaffold with Surface Modification for MSC Attachment and its Application in Circumferential Tracheal Reconstructions in Rabbit

S3 L10 Yo Kishimoto (MEMBER, Kyoto) Real-time navigation surgery for parathyroid adenoma using projection mapping with indocyanine green fluorescence

S3 L11 Joachim Hansen (GUEST, Copenhagen) Treatment with Mesenchymal Stem Cells for Xerostomia – a systematic review and meta-analysis

S3 L12 Preben Homøe (MEMBER, Køge) Recurrent Laryngeal Papillomatosis in Denmark from 1994 to 2021: A Nationwide Register Study

S3 L13 Nicola Quaranta (MEMBER, Bari) Metabolomics analysis of plasmatic markers in pediatric patients affected by OSA with and without otitis media

S3 L14 Koichiro Wasano (GUEST, Kanagawa) Potential for prevention of dementia in Japan

S3 L15 Luis Lassaletta (MEMBER, Madrid) Revisiting the Hypoglossal-Facial Nerve Transfer for Facial Reanimation in 2025. The renaissance of an old technique

S3 L16 Jeong-Whun Kim (MEMBER, Seongnam) Evaluation of Sound-Based Sleep Stage Prediction in Shared Sleeping Settings

S3 L17 Jukka Ylikoski (MEMBER, Kauniainen) How to grow old healthy

S3 L18 Masayoshi Yoshimatsu (GUEST, New York) In vivo regeneration of rat laryngeal cartilage with mesenchymal stem cells derived from human induced pluripotent stem cells via neural crest cells

S3 L19 Hiroyuki Ozawa (MEMBER, Tokyo) Genetic analysis of carotid body tumors: preliminary findings

Lunch 12.30 – 13.45

13.45 – 15.10 Session 4

Symposium: CRS Reloaded – New Mechanisms, New Medicines, New Mindsets
Chair: Philippe Gevaert (NEW MEMBER, Ghent), Marie Lundberg (GUEST, Helsinki)

Philippe Gevaert (NEW MEMBER, Ghent) Evolving Treatment Goals – From Control to Remission (15 min)

Marie Lundberg (GUEST, Helsinki) Future of surgery in the era of biologics (15 min)

S4 L1 Bradford Woodworth (NEW MEMBER, Mountain Brook) Therapeutic Potential of Ginsenoside Rb2 as a TMEM16A Potentiator in Cystic Fibrosis Sinusitis

S4 L2 Claire Hopkins (NEW MEMBER, Chislehurst) The MACRO Trial: A Randomised Controlled Trial of Clarithromycin and Endoscopic Sinus Surgery for Adults with Chronic Rhinosinusitis with and without nasal polyps

S4 L3 Claus Bachert (GUEST, Ghent) Real-world effectiveness of dupilumab in a European cohort of chronic rhinosinusitis with nasal polyps (CHRINOSOR)

S4 L4 Sanna Toppila-Salmi (MEMBER, Kuopio) ASA Treatment in CRSwNP Patients with NSAID exacerbated respiratory disease: Results from a Randomized Double-Blind Clinical Study

S4 L5 Kenichi Takano (NEW MEMBER, Sapporo) Clinical features of chronic rhinosinusitis associated with IgG4-related disease

Panel Discussion (15 min)

Fika (15 min)

15.25 – 16.05 Session 5

Symposium: Rewiring Hearing: Gene Therapy and Inner Ear Innovation
Chairs: Yehoash Raphael (MEMBER, Ann Arbor), Barbara Canlon (MEMBER, Stockholm)

S5 L1 Gary Housley (MEMBER, Sydney) Neurotrophin Gene Therapy using Bionic array Directed Gene Electrotransfer (BaDGE) of Naked DNA Encoding BDNF and NT-3 Improves Cochlear Implant Hearing Outcomes

S5 L2 Barbara Canlon (Member, Stockholm) A novel delivery procedure for inner ear gene therapy

S5 L3 Yehoash Raphael (MEMBER, Ann Arbor) Gene transfer of transcription factors induces hair cell regeneration in mature mammalian cochleae

S5 L4 Fan-Gang Zeng (MEMBER, Irvine) Treating hearing loss: from cochlear implantation to gene therapy

S5 L5 Per Caye-Thomasen (MEMBER, Copenhagen) Surgical procedure for injection of cells and substances into the human cochlear modiolus

General Assembly 16.10 – 17.10

Members' Dinner 19.00 (Posthuset – Orangeriet, Vasagatan 28, don't forget your CORLAS tie)

TUESDAY August 26th

8.00 – 9.30 Session 6

Big Ideas, Short Talks II
Otology (21 papers à 3 min and a poster)
Chair: Ann Hermansson (MEMBER, Lund)

S6 L1 Daniel Bodmer (MEMBER, Basel) A blood barrier on a chip model gives no insights into Meniere's disease

S6 L2 Orhan Ozturan (MEMBER), Istanbul) Superiorly Based Pre-/Postauricular Transposition Flap to Enlarge the External Ear Meatus in Endaural Otologic Surgery

S6 L3 Chen-Chi Wu (MEMBER, Taipei) Preliminary efficacy and safety of AK-OTOF gene therapy for OTOF-mediated hearing loss

S6 L4 Christoph Arnoldner (MEMBER, Vienna) Gene Delivery to the Inner: Overcoming Challenges and Advancing Therapies using the pig as a large animal model

S6 L5 Myrthe Hol (MEMBER, Groningen) Intra- and post-operative experiences from 51 surgeries of a new active transcutaneous bone-anchored implant system – preliminary data of follow-up Dutch patients (N=16) after 24 months

S6 L6 Marci Lesperance (MEMBER, Ann Arbor) Health care disparities and genetic hearing loss among the Amish

S6 L7 Riikka Mäkitie (GUEST, Helsinki) Otologic manifestations in Achondroplasia

S6 L8 Steven Andersen (GUEST, Copenhagen) Dynamic cone-beam CT of the middle ear - a novel concept for determining excursion of the ossicles

S6 L9 John Oghalai (MEMBER, Los Angeles) Imaging of the human inner ear with optical coherence tomography

S6 L10 Wade Chien (GUEST, Bethesda) Application of inner ear gene therapy to a Slc26a4 mutant mouse model of fluctuating hearing loss

S6 L11 Luca Verrecchia (GUEST, Stockholm) The clinical diagnosis of superior canal dehiscence syndrome

S6 L12 Jeremy Wales (GUEST, Stockholm) X-linked hearing loss – lessons learnt from long-term follow-up of a rare malformation in a single centre

S6 L13 Jong Woo Chung (MEMBER, Seoul) Peripheral Blood Cytokine Profiles in Sudden Sensorineural Hearing Loss: Potential Diagnostic and Therapeutic Implications

S6 L14 Norio Yamamoto (MEMBER, Kobe) The role of CWC27 in cochlear development

S6 L15 Judy Dubno (MEMBER, Charleston) Preliminary outcomes of a primary care hearing screening program including 5,360 older adults

S6 L16 Pascal Senn (MEMBER, Geneva) Screening for NOX3 inhibitors for the prevention of acquired sensorineural hearing loss

S6 L17 Alan Cheng (MEMBER, Palo Alto) Precise genetic control of ATOH1 enhances maturation of regenerated hair cells in the mature mouse utricle

S6 L18 Todd Mowery (GUEST, Piscataway) Superoxide Dismutase AAV gene therapy prevents cumulative hearing loss during repeated noise exposures

S6 L19 Tomas Zatoński (MEMBER, Wrocław) From Hearing to Memory: Examining the Cognitive Impact of Presbycusis in the Polish PURE Cohort

S6 L20 Johannes Ehinger (GUEST, Lund) Cochleovestibular dysfunction in patients with primary mitochondrial disease due to pathogenic mitochondrial DNA variants

Pause (10 min)

9.40 – 10.25 Session 7

The Edge of Innovation: Healing the Head and Neck
Chairs: Christian von Buchwald (MEMBER, Copenhagen), Eben Rosenthal (MEMBER, Nashville)

S7 L1 Chen-Chi Wang (MEMBER, Taichung City) Transoral Robotic Surgery and Neck Dissection for Hypopharyngeal Cancer: Long-Term Prognostic Factors and Survival Outcomes

S7 L2 René Leemans (MEMBER, Amsterdam) Surgical Salvage for HPV-associated Oropharyngeal Cancer: What is the Evidence

S7 L3 Cherie-Ann Nathan (MEMBER, Shreveport) Adjuvant Everolimus in Advanced-Stage Head and Neck Squamous Cell Carcinoma: Clinical and Preclinical Evaluation of Efficacy and Immune Modulation

S7 L4 Kathrine Kroneberg Jakobsen (GUEST, Copenhagen) Mesenchymal Stem Cells for the Treatment of Xerostomia

S7 L5 Makoto Hosoya (GUEST, Tokyo) The usefulness of Novel Continuous and Quantitative Intraoperative Facial Nerve-Monitoring System for facial nerve schwannoma surgery

Fika (15 min)

10.40 – 11.45 Session 8

Big Ideas Short Talks III
Head and Neck (15 papers à 3 min and a poster)
Chair: Cherie-Ann Nathan (MEMBER, Shreveport)

S8 L1 Remco De Bree (MEMBER, Utrecht) Image guided surgery in oral cancer

S8 L2 Antti Mäkitie (MEMBER, Helsinki) Machine learning for predicting overall survival in early-stage supraglottic laryngeal cancer: A SEER-based population study

S8 L3 Christian von Buchwald (MEMBER, Copenhagen) Nordic Oropharyngeal Squamous Cell Carcinoma Cohort

S8 L4 Krzysztof Piersiala (GUEST, Stockholm), Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma

S8 L5 Yukinori Takenaka (MEMBER, Osaka) Temporal muscle thickness as a Prognostic Factor in Patients with Head and Neck Squamous Cell Carcinoma Treated with Immune Checkpoint Inhibitors

S8 L6 Christian Grønhøj (MEMBER, Copenhagen) Specificity and sensitivity of circulating HPV-DNA in patients with oropharyngeal squamous cell carcinoma

S8 L7 Wendell Yarbrough (MEMBER, Chapel Hill) Turning the bad tumors good: Systemic treatment to switch HPV+ HNSCC subtype and sensitize resistant tumors to radiation

S8 L8 Mizuo Ando (MEMBER, Okayama) Changes in the tumor microenvironment in Near-infrared photoimmunotherapy

S8 L10 Kenji Kondo (MEMBER, Tokyo) Assessing volume growth of paranasal sinuses and nasal cavity in children using three-dimensional imaging software

S8 L11 Giovanni Almadori (MEMBER, Rome) The role of PTHrP and PTH1R expression in locally advanced laryngeal squamous cell carcinoma: prognostic implications and response to cetuximab therapy

S8 L12 Carter Van Waes (MEMBER, Annapolis) Functional RNAi Screening I dentifies G2/M and Kinetochore Components as Modulators of TNFa/NF-kB Prosurvival Signaling in Head and Neck Squamous Cell Carcinoma

S8 L13 Taku Yamashita (MEMBER, Sagamihara) The role of REV7, CD109, and midkine as biomarkers in head and neck cancer

S8 L14 Matteo Alicandri Ciufelli (MEMBER, Modena) Effectiveness of Neuromuscular Retraining (NMR) in patients with hypoglossal-facial anastomoses

S8 L15 Hani Marzouki (MEMBER, Jeddah) Advanced surgical and medical treatment of medullary thyroid cancer

Pause (5 min)

11.50 – 12.45 Session 9

Big Ideas Short Talks IV
Cochlear Implants (11 papers à 3 min and a poster)
Chair: Antti Aarnisalo (MEMBER, Helsinki)

S9 L1 Piotr Skarżyński (MEMBER, Warsaw) Local Delivery of Steroids to the Inner Ear via the Medical Device INCAT (Inner Ear Catheter) in Partial Deafness Patients During Cochlear Implantation – Preliminary Results and a Feasibility Study

S9 L2 Jae-Jin Song (GUEST, Seongnam) Molecular imaging-based machine learning predicts cochlear implant outcome in prelingually deaf children

S9 L3 Marco Caversaccio (MEMBER, Bern) Do Expert Surgeons Perform Better CI surgery? Evidence from an In Vitro Study of 30 International CI Surgeons

S9 L4 Craig Buchman (MEMBER, St Louis) Intensity-Driven Shifts in Tonotopic Coding in Humans: A Framework for Cochlear Implant Frequency Allocation

S9 L5 Aarno Dietz (MEMBER, Kuopio) Robotic Electrode Insertion Reduces Trauma in a Cadaveric Cochlear Model

S9 L7 Theodore Mcrackan (GUEST, Charleston) Enhancing Pre-Cochlear Implant Counseling Using the Cochlear Implant Quality of Life (CIQOL) Instrument Suite

S9 L8 Hong Ju Park (MEMBER, Seoul) Cortical Volumetric Changes before and after Cochlear Implantation in Postlingually Deaf Adults

S9 L9 Adrien A Eshraghi (MEMBER, Miami) Drug Y Eluting Electrode Provides Otoprotection in a Preclinical Rat Model of Cochlear Implantation

S9 L10 Yann Nguyen (MEMBER, Paris) Robotic-Assisted Insertion of Cochlear Implant CI632: an ex-vivo study

S9 L11 Marlan Hansen (MEMBER, Iowa City) Modulation of immune/inflammatory responses to cochlear implantation in animals and humans

Lunch 12.45 – 13.50

13.50 – 14.45 Session 10

Unraveling Ear Disease: Genetic Drivers and Structural Defenses
Chairs: Claes Möller (MEMBER, Örebro), Ann Hermansson (MEMBER, Lund)

S10 L1 Vincent Van Rompaey (NEW MEMBER, Edegem) Functional Outcome in a Rationally Designed Genomically Humanized Mouse Model for Dominantly Inherited Hearing Loss DFNA9

S10 L2 Regie Santos-Cortez (MEMBER, Aurora) Rare and low-frequency genetic variants in families with otitis media

S10 L3 Allen F Ryan (MEMBER, Solana Beach) Regulation of mucin genes by chromatin accessibility during otitis media

S10 L4 Byung Yoon Choi (MEMBER, Seongnam) Otof gene transfer in DFNB9 mice carrying human founder non- truncating alleles

S10 L5 Karl-Bernd Hüttenbrink (MEMBER, Düsseldorf) Retraction of the tympanic membrane: is it an active self-defense mechanism? A new concept and its surgical implications against recurrency

S10 L6 Diego Preciado (NEW MEMBER, Washington) Micro RNAs Implication in the Progression of Otitis Media

Pause (5 min)

14.50 – 15.30 Session 11

Otology
Chairs: Marcos Goycoolea (MEMBER, Santiago), Sten Hellström (MEMBER, Stockholm)

S11 L1 Jesper Hvass Schmidt (NEW MEMBER, Odense) Can Hearing Aids Mitigate the Risk of Dementia in Older Adults with Hearing Loss?

S11 L2 Tatsuo Matsunaga (MEMBER, Tokyo) A wide spectrum of rare causative genes identified by whole exome sequencing and phenotype similarity search in undiagnosed patients with syndromic hearing loss

S11 L3 Kimitaka Kaga (MEMBER, Tokyo) A Case of Michel Type Deformity in the Inner Ear Anomaly-Long Term Fellow Up of a Two-months-old Child to Age Twenty

S11 L4 Saku Sinkkonen (MEMBER, Helsinki) Facial Nerve Stimulation in Otosclerosis Patients with Cochlear Implants – The Impact of Lateral versus Perimodiolar Electrode Array Positioning

S11 L5 Elisabetta Zanoletti (MEMBER, Padova) The role of vasculature of the internal auditory canal and functional surgery of vestibular schwannoma

Fika (10 min)

15.40 – 17.05 Session 12

Symposium: CI in the Real World: Syndromes, Side Effects, and Cognitive Impact
Chairs: P. Ashley Wackym (MEMBER, New Brunswick), Hans-Peter Zenner (MEMBER, Tübingen)

S12 L1 Nicolas Verhaert (NEW MEMBER, Leuven) Bio-sensing for cochlear implant-induced trauma: new developments

S12 L2 Antti Aarnisalo (MEMBER, Helsinki) Variable inner ear pressure changes associated with manual electrode insertion; a temporal bone study

S12 L3 Kadir Serkan Orhan (MEMBER, Istanbul) A Novel Surgical Technique in Bilateral Cochlear Implantation

S12 L4 David Horn (NEW MEMBER, Seattle) Maturation of frequency resolution in infants who use cochlear implants

S12 L5 Bruce Gantz (MEMBER, Iowa) Acoustic Hearing Preservation Manual vs Robotic Cochlear Implant Insertion: Rates of Long-Term Delayed Hearing Loss

Pause (5 min)

S12 L6 Abdulrahman Hagr (MEMBER, Riyadh) Adult Simultaneous Cochlear Implantation: Local Anesthesia

S12 L7 Giorgia Girotto (NEW MEMBER, Trieste) Beyond the curtains of Non-syndromic Hereditary Hearing Loss (NSHHL): Whole Exome Sequencing (WES) reveals the presence of Non-Syndromic Mimics (NSMs)

S12 L8 Richard Smith (MEMBER, Iowa City) The Contribution of Common Variants in Deafness-Associated Genes to Age-Related Hearing Loss

S12 L9 Wolfgang Baumgartner (MEMBER, Vienna) Update in Robotic Cochlear Implantation – HEARO & OTODRIVE

S12 L10 Pim Van Dijk (MEMBER, Groningen) GABA inhibition in humans with tinnitus

Cultural Evening, Stockholm City Hall at 19.00, Hantverkargatan 1

WEDNESDAY August 27th

08.00 – 09.00 Session 13

Silent Voices and Sleepless Nights: Rebuilding Airway Function
Chairs: Koichi Omori (MEMBER, Kyoto), Jussi Jero (MEMBER, Helsinki)

S13 L1 Ihab Atallah (NEW MEMBER, Grenoble) Innovations in the Management of Unilateral Vocal Fold Paralysis: Expanding Therapeutic Possibilities

S13 L2 Miro Tedla (MEMBER, Bratislava) Novel surgical approach to address posterior glottic stenosis

S13 L3 Yoon Se Lee (MEMBER, Seoul) Establishment of humanized mouse models in the evaluation of PD-1/PD-L1-axis blockade-based head and neck cancer immunotherapy

S13 L4 Alexander Hillel (NEW MEMBER, Baltimore) E-cadherin-deficient epithelium creates a leaky barrier and promotes fibrosis in idiopathic subglottic stenosis

S13 L5 Maria Suurna (MEMBER, Miami) Outcomes of Bilateral Hypoglossal Nerve Stimulation for Treatment of Sleep Apnea

S13 L6 Olivier M Vanderveken (NEW MEMBER, Edegem) The Effect of Hypoglossal Nerve Stimulation on Sleep Apnea Specific Hypoxic Burden in patients with Obstructive Sleep Apnea

Pause (15 min)

09.15 – 10.10 Session 14

Big Ideas, Short Talks V
Miscellaneous (11 papers à 3 min and a poster)
Chair: Lars Olaf Cardell (MEMBER, Stockholm)

S14 L1 Antje Welge-Lüssen (MEMBER, Basel) Visiting a Smell and Taste Clinic with uni- or bilateral normosmia

S14 L2 David Housley (GUEST, Melbourne) Impact of Management Decisions on Outcomes of Paediatric Subperiosteal Orbital Abscess: A Retrospective Study

S14 L3 Per Gisle Djupesland (MEMBER, Oslo) Nasal Dilators in Sports Activities – Magic or Gimmick?

S14 L5 Masafumi Sakashita (GUEST, Fukui) A Comprehensive Analysis of Big Data on Health Observations Concerning Cedar Pollinosis Among Youth in Fukui, Japan

S14 L6 Cem Meco (MEMBER, Ankara) Periorbital suspension and the role of anterior ethmoidal artery during endonasal endoscopic access to the lateral frontal sinus and skull base

S14 L7 Philippe Gevaert (NEW MEMBER, Ghent) Clinical and Proteomic Analysis of Biologic Treatments in CRSwNP: Real-World Insights from a Belgian Cohort

S14 L8 Andro Košec (MEMBER, Zagreb) Salivary cortisol concentration is an objective measure of the physiological response to acute stress caused by loud music

S14 L9 Sébastien Schmerber (MEMBER, Grenoble) Skull Vibration Induced afternystagmus - a new clinical indicator of anterior canal dehiscence

S14 L10 Georgios Mantokoudis (MEMBER, Bern) Gaze Position Error During Head Impulses as a Predictor of Symptom Severity in Subacute Dizzy Patients

S14 L11 Jeffrey Harris (MEMBER, San Diego) Vaccine Hesitancy as a Risk Factor for Otologic Dysfunction Following SARS-CoV-2 Infection

Fika (15 min)

10.25 – 11.45 Session 15

Signals from the Labyrinth: Hearing and Balance in Focus
Chairs: Måns Magnusson (MEMBER, Lund), D. Bradley Welling (MEMBER, Boston)

S15 L1 Sofia Waissbluth (NEW MEMBER, Santiago) Understanding Bilateral Vestibulopathy: Insights from the Video Head Impulse

S15 L2 Powen Cheng (MEMBER, New Taipei City) The relationship between the betahistine treatment duration in patients with cochlear MD and their clinical outcomes

S15 L3 Tadashi Kitahara (MEMBER, Kashihara) Prognosis of asymptomatic endolymphatic hydrops in healthy volunteers: A five-year cohort study

S15 L4 Shinichi Iwasaki (MEMBER, Nagoya) Double-blind placebo-controlled crossover study of the effect of prolonged noisy galvanic vestibular stimulation on posture in vestibulopathy

S15 L5 Dirk Beutner (NEW MEMBER, Göttingen) Partial ossicular reconstruction with a novel balljoint prosthesis

S15 L6 Stefan Plontke (MEMBER, Halle) Inner ear Schwannomas: Preservation of vestibular function and hearing rehabilitation with cochlear implants after surgical tumour removal – our experience in a monocentric case series of 133 patients

S15 L7 Sharon Cushing (NEW MEMBER, Toronto) Solving for Why? Impact of Early Etiologic Assessment on the Access to Bilateral Cochlear Implantation in Children with Hearing Loss

S15 L8 Jeong Hun Jang (NEW MEMBER, Suwon) Sialyllactose preserves residual hearing after cochlear implantation

S15 L9 Yen-Fu Cheng (NEW MEMBER, Taipei) CRISPR Exon Skipping for Pendred Syndrome (DFNB4) Hearing Loss: Vestibular Function Restored but Hearing Loss Persists in a Mouse Model

Pause (15 min)

12.00 – 12.35 Session 16

Smell, Sight, and Survival: High-Stakes Rhinology
Chairs: Matti Anniko (MEMBER, Uppsala), Markus Rautiainen (MEMBER, Tampere)

S16 L1 Stephan Hackenberg (NEW MEMBER, Wurzburg) Metabolization of odorants by human nasal mucosa – a crucial step in olfaction

S16 L2 Andrzej Sieskiewicz (NEW MEMBER, Biatystok) Standardized Endoscopic Optic Nerve Decompression: A Comprehensive Radiological and Anatomical Study

S16 L3 Romain Kania (MEMBER, Paris) Radical Endonasal Surgery Combined with Liposomal Amphotericin B for the Treatment of rhino-orbito-cerebral mucormycosis (ROCM): The MICCA Protocol

S16 L4 Ola Sunnergren (NEW MEMBER, Jönköping) What's good enough in septoplasty?

LUNCH 12.35 – 13.50

13.50 – 15.10 Session 17

Vision for the Future from the CORLAS Experience
Chairs: Barbara Wollenberg (MEMBER, Munich), Shakeel Saeed (MEMBER, London)

S17 L1 Måns Magnusson (MEMBER, Lund) Meniere's disease: different mechanisms for hydrops and implication of treatments – an update

S17 L2 Anil Lalwani (MEMBER, Scarsdale) Novel dual-lumen microneedle delivers adeno-associated viral vectors in the guinea pig inner ear via the round window membrane

S17 L3 Anna Rita Fetoni (MEMBER, Naples) Linking oxidative stress and inflammation in hearing loss: A journey from the cochlea to the brain

S17 L4 Karen Avraham (MEMBER, Tel Aviv) Genetics of deafness: Implications for precision medicine

S17 L5 Stephen O'Leary (MEMBER, Melbourne) Perilymphatic sampling transcriptomics informs the biology of high electrode impedance after cochlear implantation

S17 L6 Nicole Rotter (MEMBER, Mannheim) Update on cartilage tissue engineering in otorhinolaryngology

S17 L7 Andrej Kral (MEMBER, Hannover) Predicting outcomes following cochlear implantation: Assessment of cochlear health

Discussion (15 min)

CLOSING CEREMONY 15.10 – 15.25

Gala Dinner, Operakällaren – Operaterrassen at 19:00, Karl XII:s torg 1

S1 L1

Artificial Intelligence in Oto-Rhino-Laryngology: From Vision to Real-World Integration

Stephan Lang[1], Nadia Sadok[1], Eric Deuß[1], René Hosch[2], Merlin Engelke[2], Jens Kleesiek[2], Felix Nensa[2]
[1] Dept. of Oto-Rhino-Laryngology, University Hospital Essen, [2] Institute for Artificial Intelligence in Medicine, University Hospital Essen

Background:

Artificial Intelligence (AI) is reshaping otorhinolaryngology across the entire clinical spectrum. At our University-Hospital, we are working on an AI-powered ecosystem in collaboration with the Institute for Artificial Intelligence in Medicine (IKIM) that integrates diagnostics, therapy planning, and surgical execution into a seamless digital workflow.

Material and Methods:

Our approach uses high-performance AI algorithms based on machine learning techniques and trained on large-scale, multimodal datasets. By leveraging deep neural networks and explainable AI models, we create predictive tools that continuously improve with data and integrate seamlessly into clinical workflows.

Results:

Our project Smart Precision Surgery exemplifies this approach, combining AI-based preoperative risk assessment, automated intraoperative instrument detection, and real-time surgical phase recognition. This is providing the base for a fully automated, data-rich surgical workflow. Additionally, our AI-enhanced tumor dashboard supports tumor board preparation with guideline-based therapy suggestions. These efforts have been complemented by a recent publication in Nature Cancer demonstrating the prognostic power of our neural network model across multiple cancer types, stratifying over 7,800 patients into clinically meaningful risk categories. In parallel, our team contributes to the EU-funded IDEA4RC project, which aims to build a smart ecosystem for the governance, sharing, and reuse of health data in rare cancers. The initiative promotes secure cross-border collaboration and data harmonization to improve care for patients with rare tumors.

Conclusion:

AI-driven tools are already reshaping clinical practice in ENT. Our integrated ecosystem demonstrates how AI can sustainably improve surgical precision, patient safety, and personalized treatment across the entire continuum of care.

S1 L2

Genetic Diagnosis and Discovery Enabled by Large Language Models

Konstantina Stankovic[1], Tao Tu[2], Khaled Saab[2], Weida Liu[3], Zhouqing Fang[3], Zhuanfen Cheng[3], Svetolik Spasic[1], Maja Djurisic[1], Hiroaki Mohri[1], Wenlong Ren[3], Anil Palepu[2], Juraj Gottweis[4], Alan Karthikesalingam[4], Kavita Kulkarni[4], Annalisa Pawlosky[4], Devon Bonner[5], Elijah Kravets[5], Shruti Marwaha[6], Hector R. Mendez[5], Matthew T. Wheeler[7,8], Jonathan A. Bernstein[5,8], Cheng-Yu Tsai[9,10], Chen-Chi Wu[9,10,11,12], Vivek Natarajan[4], Gary Peltz[3]

[1] Department of Otolaryngology – Head and Neck Surgery, Stanford University School of Medicine, Stanford CA, [2] Google DeepMind, Mountain View, CA, [3] Department of Anesthesiology, Pain and Perioperative Medicine Stanford University School of Medicine, Stanford CA; , [4] Google Research, Mountain View CA, [5] Stanford Center for Undiagnosed Diseases, [6] Stanford Center for Undiagnosed Diseases, , [7] Department of Medicine, Stanford University School of Medicine, Stanford CA, [8] Department of Pediatrics, Stanford University School of Medicine, Stanford, CA, [9] Department of Otolaryngology, National Taiwan University College of Medicine, 100233 Taipei, Taiwan, [10] Department of Otolaryngology, National Taiwan University Hospital, 100225 Taipei, Taiwan, [11] Department of Medical Research, National Taiwan University Hospital Hsin-Chu Branch, Hsinchu 302041, Taiwan, [12] Department of Otolaryngology, National Taiwan University Hospital Hsin-Chu Branch, Hsinchu 302041, Taiwan

Background: Artificial intelligence (AI) has been used in many areas of medicine, and large language models (LLMs) have shown potential utility for various clinical applications.

Materials and Methods: To determine if LLMs can be used to accelerate the pace of genetic diagnosis and discovery, we examined, in mice and humans, whether recently developed LLMs (Med-PaLM 2 and Med-Gemini), which were specialized for biomedical applications, could perform these tasks. Knockin-in mice were generated to test LLM predictions.

Results: In response to free-text input, Med-PaLM 2 correctly identified murine genes with the experimentally verified causative genetic factors for six previously studied murine models for biomedical traits. Med-PaLM 2 also analyzed a list of genes with genetic variants produced by comparative analysis of murine genomic sequences, and it identified a novel causative murine genetic factor. This led to a digenic model for susceptibility to spontaneous hearing loss that was validated using knock-in mice. Med-Gemini analyzed a large list of genes with genetic variants in the genomic sequences of 20 human subjects with hearing loss; and it identified causative genetic factors for hearing loss in 80%, and high-risk variants in 10%. It also identified causative genetic factors for three subjects with multi-faceted manifestations of suspected genetic diseases, which required 14 to 34 different terms to describe their symptom complex.

Conclusion: Our results demonstrate that medically specialized LLMs can facilitate genetic diagnosis and discovery in mice and humans.

S1 L3

From larynx to brain: AI-based diagnostics of neurological voice disorders

Kristina Simonyan[1]

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Nearly 8% of U.S. adults experience voice issues, making voice disorders one of the leading forms of communication disability. Among these, neurological voice disorders, laryngeal dystonia (LD) and voice tremor (VT), have complex and commonly overlapping symptomatology. The lack of objective diagnostic biomarkers and the subsequent absence of a gold standard test leads to as low as 34% diagnostic agreement between expert clinicians.

We developed machine-learning algorithms 1) to automatically identify a neural biomarker for LD diagnosis using structural brain MRIs (DystoniaNet) and 2) to predict symptom severity based on voice recordings (NeuroVoiceNet). We tested these algorithms in a large cohort of patients (589 for DystoniaNet and 675 for NeuroVoiceNet).

Using convolutional neural network architecture, DystoniaNet achieved 91.3% accuracy in distinguishing LD and VT. The algorithmic decision was based on the discovery of a neural biomarker of differential diagnosis, including regions of the basal ganglia, thalamus, cerebellum, and white matter tracts. Using a transformer multi-task model, NeuroVoiceNet predicted the symptom severity of LD and VT with 90.2% accuracy based on the identification of disorder-characteristic voice breaks, strain, breathiness, or tremor.

DystoniaNet and NeuroVoiceNet demonstrated superior performance in differentially diagnosing neurological voice disorders and determining the severity of symptoms. Both AI algorithms exceeded the currently existing clinical workflow paradigms, both in terms of accuracy and time to diagnosis. DystoniaNet and NeuroVoiceNet have high translational potential as objective AI platforms for the clinical management of LD and VT to help accelerate the timely diagnosis and treatment of these patients.

S1 L5

Better speech understanding and subjective experience with a novel artificial intelligence-based dereverberation algorithm in cochlear implant users

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Background:

Speech understanding with cochlear implants (CIs) is challenging in environments with reverberation. This study examined the impact of AI-based dereverberation algorithms on speech understanding for CI users.

Materials and Methods:

15 CI users participated, each acting as their own control. Two algorithms were tested: one focused on late reverberation (algo1), and another on both late and early reverberation (algo2). The effectiveness of these algorithms was assessed using the Dutch/Flemish Matrix Test, a sentence test with the percentage of correctly understood words as the outcome measure. Six different conditions were tested: clean speech (without reverberation), clean speech with algo1 or algo2, reverberant speech, and reverberant speech with algo1 or algo2. Reverberation times between 0.4 and 1.5 seconds were included in the study. In addition, subjective assessments of sound quality (three different scales) were carried out.

Results:

Algo1 improved speech understanding in reverberation by an average of 11% ($p<0.001$), and algo2 by 17% ($p<0.001$). The benefit of algo2 was significantly greater than that of algo1 ($p = 0.018$). Neither algorithm had a significant effect on speech understanding in the absence of reverberation ($p = 1.00$). Subjectively, participants rated speech processed by both algorithms as more pleasant than reverberant speech without any algorithms.

Conclusion:

Both reverberation reduction algorithms provide benefits for CI users in terms of speech intelligibility and perceived sound quality. Since the algorithms had no effect on clean speech, they can remain continuously active, even in non-reverberant environments.

S2 L1

Long-term results of sentinel node biopsy for early oral and oropharyngeal squamous cell carcinoma

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Background

To evaluate the long-term oncologic outcomes of sentinel node biopsy (SNB) in early (T1/T2) oral and oropharyngeal squamous cell carcinoma (OOSCC) based on a two-center retrospective analysis. Primary endpoints were neck control rate and survival outcomes.

Material and Methods

A retrospective analysis of a originally prospectively enrolled cohort was conducted at the University Hospital Zurich (USZ, 2003-2007) and the Cantonal Hospital St. Gallen (KSSG, 2008-2022). A total of 186 patients (USZ: 69, KSSG: 117) with clinically node-negative early OOSCC underwent SNB. Sentinel detection was performed using preoperative lymphoscintigraphy, single photon emission computed tomography (SPECT/CT), and intraoperative gamma probe detection. Neck recurrence, disease-specific survival (DSS), and sentinel detection rate were analyzed.

Results

The sentinel detection rate was 98.9%. Positive sentinel nodes were found in 60 patients (32.5%). At five years, the neck recurrence rate after SNB was 10%. The five-year DSS was 94.8% (95% CI: 91.1%-98.6%) and was significantly higher in patients with negative sentinel nodes.

Conclusion

SNB remains a highly effective staging tool for early OOSCC, providing excellent long-term oncologic outcomes. Patients with negative sentinel nodes demonstrate superior DSS and favorable neck control rates, reinforcing SNB as a reliable alternative to elective neck dissection. However, the prognostic significance of micrometastases and isolated tumor cells remains unclear.

S2 L2

Sentinel node-assisted neck dissection in N+ oral squamous cell carcinoma

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Background:

Neck recurrence rates remain elevated in patients with node-positive (N+) oral squamous cell carcinoma (OSCC), indicating that conventional neck dissection (ND) may not reliably eradicate all lymph nodes harbouring occult metastases. Although sentinel lymph node biopsy (SLNB) is a well-established modality for staging and therapeutic guidance in early-stage (T1–T2, N0) OSCC, its role in the management of N+ disease remains insufficiently defined. This study aimed to investigate lymphatic drainage patterns and determine the frequency of additional metastatic sentinel nodes (SN+) beyond those identified by clinical and radiological evaluation in patients with N+ OSCC.

Materials and Methods:

In this retrospective study, 54 patients with clinically staged T1–T4 N+ OSCC who underwent neck dissection supplemented by sentinel lymph node biopsy (SLNB) between 2020 and 2025 were included. The SLNB protocol combined SPECT-CT with indocyanine green fluorescence and gamma probe detection. Following pathological evaluation, 37 patients were confirmed to have nodal metastases (pN+).

Results:

Among all pN+ patients, contralateral drainage occurred in 19/38 (50%) with a higher rate in cT3-T4 (8/20, 40.0%) and pN2a-N3b (12/23, 52,2%) compared to tumours cT1-T2 (9/17, 52.9%) and pN1 (2/10, 20%). Overall, SN+ in addition to known metastasis was detected in 15/38 (39.5%) patients, including 7 (18.4%) with contralateral SN+.

Conclusion:

SLNB–assisted neck dissection in patients with N+ OSCC enhances the detection of occult metastases and may provide more accurate staging, and potential for improved regional disease control.

S2 L3

Accuracy and prognosis of extranodal extension on radiologic imaging in HPV+ oropharyngeal cancer: the multinational HNCIG-EPIC iENE study.

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Background:

Extranodal extension on radiology(iENE) is reported in single-centre studies to be negatively prognostic in Human papillomavirus-mediated oropharyngeal cancer (HPV+OPC) and is a major eligibility criterion for surgical treatment. However, studies report widely varying sensitivities, specificities and interobserver correlation. In this research the prognostic power, sensitivity and specificity of iENE in HPV+OPC in real-world practice are determined.

Methods and Materials:

A retrospective cohort of 821 consecutive subjects with p16+OPC, treated with surgery and/or chemoradiotherapy(CRT), from 13 multinational secondary hospitals in nine countries was analysed. Main outcomes were sensitivity, specificity and overall survival(OS).

Results:

109/394(27.7%) with no iENE had ENE on histopathology(pENE), and 109/192(56.8%) patients with pENE were misclassified as having no iENE. iENE sensitivity and specificity were 44.5%(95%CI: 37.8-51.4%) and 87.6%(95%CI: 84.1-90.6%) respectively, and varied significantly between centres. Negative predictive value was 75.3% (95% CI 72.3-77.5%).

Subgroup analyses showed significantly increased sensitivity and specificity if patients had both CT and MRI: 84.6%(95%CI: 65.1-95.6%, p<0.001) and 94.5%(95%CI: 82.3-99.4%, p=0.022) respectively. Specialist radiologists showed better specificities (89.14%(85.69-91.99%) vs 46.67%(21.27 -73.41%), p<0.001) to non-specialists.

On multivariable analysis, iENE positivity was not a statistically significant independent predictor of OS (adjusted hazards ratio(aHR) 1.50(95%CI: 0.97-2.32, p=0.071). Two proposals for amended TNM staging did not yield large improvements.

Conclusion:

In current real-world practice, iENE showed widely varying and modest accuracy, and was not independently prognostic of outcomes in HPV +OPC.. iENE accuracy and prognostic power increased significantly by using combined CT and MRI scanning, and specialist radiologists. Clinicians should be cautious about making treatment decisions based on iENE.

S2 L4

Surgeon-performed head and neck ultrasound in office-based and perioperative setting

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Background

Head and neck ultrasound has traditionally been performed in the radiology department, but it is now expanding to office□based and surgical settings. In Denmark, otolaryngologists use ultrasound as an extension of the clinical examination to ensure faster diagnostic workup, guide biopsies, and perform minimally invasive treatments. This presentation will focus on how ultrasound can be integrated into ENT clinical practice and how more advanced ultrasound techniques can advance surgical care.

Material and Methods

Data from 320 patients from four unpublished studies (one retrospective study and three prospective clinical trials) about the use of otolaryngologist-performed ultrasound from the Departments of Otorhinolaryngology, Head and Neck Surgery at Rigshospitalet, Zealand University Hospital, and Aarhus University Hospital, Denmark, will be presented.

Results

A retrospective study of 119 patients found that one-stop surgeon-performed fine-needle biopsies (FNA) can achieve the same diagnostic results as radiologists-performed FNA but significantly shorter time to diagnose head and neck cancer. A prospective multicenter trial involving 162 patients found that surgeon-performed transoral US can improve the diagnostic accuracy and staging of oropharyngeal cancer compared to clinical exams and MRIs. Another two clinical trials, including 30 and 9 patients with tongue and oropharyngeal cancer, found that 3D perioperative ultrasound can be used perioperatively to detect 78% and 80% of cases with close surgical margins during surgery, respectively.

Conclusion

Implementation of surgeon-performed head and neck ultrasound can improve patient management in an office-based and perioperative setting.

S2 L5

Impact of Tumor Volume on Gastrostomy Use and Mortality in Advanced Laryngeal Cancer

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Background: To investigate the predictive role of tumor volume in the use of gastrostomy tubes and mortality in patients with advanced laryngeal and hypopharyngeal cancer.

Methods: A multi-institutional cohort study involving 41 head and neck cancer centers across North America included patients with newly diagnosed advanced squamous cell carcinoma of the larynx (cartilage-invading T3, T4) or hypopharynx (T2, T3) for which curative treatment was planned. Tumor characteristics and treatment were recorded alongside functional status and patient-reported outcomes. Imaging was reviewed by a single head and neck cancer neuroradiologist.

Results: Of an original cohort of 279 patients, 156 patients had imaging available for review. Patients were predominantly male (74%) with laryngeal primary tumors (88%). Mean age was 65.2 years. Fifty-nine percent underwent primary surgical laryngectomy or laryngopharyngectomy while 41% were treated with primary chemoradiation. Multiple logistic regression demonstrated that treatment modality (chemoradiation vs. surgery) and tumor volume were the most important independent predictors.

Patients undergoing chemoradiation had a higher likelihood of requiring a gastrostomy [OR 4.00, P<0.002]. Tumor volume also independently predicted gastrostomy use, with a 4% increased risk of gastrostomy per 1 mL increase in tumor volume [p<.03]. Variables that were not predictive of gastrostomy included T stage, N stage, and anatomic site (hypopharynx vs larynx). Additionally, tumor volume was predictive of 12-month mortality, with a 6.3% risk of higher 12-month mortality with each 1 mL of tumor volume increase.

Conclusions: Tumor volume should be considered as a predictor for both gastrostomy use and mortality.

S2 L6

First Experience with the DaVinci SP Robotic System in Germany: Opportunities and Challenges in Head and Neck Surgery

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Background: Robotic-assisted surgery has significantly advanced treatment options in head and neck procedures, particularly in anatomically confined regions like the pharynx and larynx. The DaVinci SP (Single Port) system is a state-of-the-art platform designed for such complex areas, offering improved access, precision, and visualization through a single, flexible port. While its clinical value is recognized internationally, the implementation of robotic surgery in Germany remains limited.

Methods: In 2024, University Medicine Greifswald became one of the first institution in Germany to introduce the DaVinci SP system. The integration process involved substantial logistical coordination, tailored training programs for surgical and support teams, and modification of existing clinical pathways. This introduction was conducted without standard reimbursement support, relying instead on institutional funding.

Results: Successful implementation of the DaVinci SP system required not only clinical adaptation but also navigation of systemic barriers. Unlike countries where robotic surgery is well-integrated into healthcare financing, the German Diagnosis-Related Group (DRG) system currently does not provide specific reimbursement for robotic-assisted procedures. This creates significant financial hurdles for adoption, particularly in non-private hospital settings.

Conclusion: This first experience with the DaVinci SP in Germany highlights both the technical advantages of the platform and the institutional commitment required to overcome systemic limitations. Broader adoption of robotic surgery in Germany will depend on changes in reimbursement policies and increased recognition of the long-term value of minimally invasive approaches in complex head and neck procedures.

S3 L1

Competence-based Otolaryngology Resident Training – National Perspectives

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Background: Competency-Based Medical Education (CBME) emphasizes workplace-based assessments, yet factors influencing competency attainment remain underexplored. Since 2020, Taiwan Society of Otorhinolaryngology Head and Neck Surgery (TSOHNS) has develped 11 Entrustable Professional Activities (EPAs) to implement via a digital EMYWAY platform (2022). We report the effectiveness of nationwide EPA adoption in otolaryngology resident training.

Methods: A total of 9,345 EPA assessments data (2022-2023, performed by 274 residents and 362 faculty across 34 programs) from EMYWAY plateform are retrieved for analysis. Multivariate regression is applied to identify factors affecting attainment of expected entrustment-supervision levels by postgraduate year.

Results: Overall, 68.2% of assessments met expected entrustment-supervision levels. Factors negatively associated included training in urban hospitals (OR=0.50, 95% CI 0.43–0.60), advanced case complexity (OR=0.44, 95% CI 0.40–0.49), surgical procedures (OR=0.40, 95% CI 0.34–0.46), and senior residency years (R4: OR=0.29, 95% CI 0.24–0.35; R5: OR=0.11, 95% CI 0.09–0.13). Conversely, emergency settings attribute to higher achievement level (OR=4.83, 95% CI 3.70–6.31).

Conclusion: It shows that urban hospitals, complex clinical scenarios, surgical contexts, and senior residency training may negatively impact the training effectiveness. Intensive clinical exposure may explain the higher achievement in emergency settings. Future longitudinal research should assess long-term impacts on clinical proficiency and patient outcomes.

Keywords: competency-based medical education (CBME), entrustable professional activities (EPAs), otolaryngology

S3 L2

Toward A Wearable Device for Facial Pacing

Tessa Hadlock, Roy Xiao

Background: We hypothesized that near-synchronous movement could be restored to non-flaccid facial paralysis (NFFP) patients through a wearable device that detects specific healthy-side facial movements and stimulates appropriate contralateral movements. We applied EyeEcho, a non-invasive ultrasonic acoustic-reflection-based sensing system, to detect healthy-side facial movements. Separately, we triggered near-symmetric movements in unilateral NFFP patients using transcutaneous functional electrical stimulation (FES). These data advance our efforts toward a wearable closed-loop facial pacing device.

Materials/Methods: We used EyeEcho glasses to record dynamic facial contour data from 26 patients with unilateral NFFP and assessed facial expression detection accuracy compared with simultaneous, ground truth infrared-based TrueDepth video recordings. We applied electrical pulse trains to NFFP patients and compared FES-elicited motions with volitional movement attempts using eFACE and Emotrics. We assessed stimulation tolerability using the Wong-Baker FACES scale.

Results: Facial expressions and side-to-side asymmetries recorded by acoustic reflections versus infrared videography were highly similar, validating the EyeEcho for unobtrusive facial movement tracking. FES-elicited brow elevation matched healthy-side excursion in 32 NFFP patients. Likewise, transcutaneous FES achieved complete eye closure (eFACE score 100) in patients with incomplete voluntary closure (n=12) and meaningful lower lip excursion in 90% of patients with lower lip asymmetry (n=9) - all at current levels that participants described as tolerable for daily FES.

Conclusions: EyeEcho can accurately detect asymmetric facial movements, and transcutaneous FES can restore desired movements in multiple regions with tolerable current levels. These facial movement detection and stimulation findings provide a strong foundation for developing a closed-loop facial pacing system.

S3 L3

Bi-layered Microflap Technique for the Treatment of Anterior Glottic Web

Background

Anterior glottic webs are an epithelium-covered fibrous tissue at the anterior commissure, leading to synechia of bilateral vocal folds. It manifests with symptoms ranging from hoarseness to airway obstruction. However, treating anterior glottic web is challenging due to its high recurrence rate. In this study, we reported our treatment outcomes using bi-layered microflap technique.

Materials and Methods

This retrospective cases series enrolled 10 cases with anterior glottic web from an tertiary medical center. All the patients received bi-layered microflap technique for the treatment of anterior glottic web under the setting as microlaryngeal surgery. Primary treatment outcome was the web length ratio (in reference to vocal fold), while the secondary outcomes included voice handicap index (VHI-10), smoothed cepstral peak prominence (CPPs), and GRB scores.

Results

The ten patients comprised six men and four women. Their ages ranged between 32 and 77 years with a mean of 51.4 years. The average web length ratio decreased from 56.6±19% to 33.7±13.8%. VHI-10 scores improved from 31.6±7.2 to 18.6±11.0. CPPs increased from 6.5±3.0 to 7.7±3.6, and GRB scores decreased from 5.5±0.9 to 4.0±1.9.

Conclusion

Bi-layered microflap technique is an effective method for managing anterior glottic web. This single-stage, stent-free endoscopic procedure achieved 70~80% success rate depending on different outcome parameters, exhibiting both structural and functional improvements.

S3 L4

Ultrasonographic Changes of Upper Airway Structures in Children with Obstructive Sleep Apnea after Adenotonsillectomy

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Background: Adenotonsillar hypertrophy is a major cause of pediatric obstructive sleep apnea; however, up to 75% of post-adenotonsillectomy patients still show polysomnographic alterations. We evaluated ultrasonographic changes in upper airway structures after adenotonsillectomy and their associations with sleep parameters.

Materials and Methods: We assessed 55 children (<18 years) with sleep-disordered breathing (14: primary snoring, 41: obstructive sleep apnea) who underwent polysomnography and upper airway ultrasonography before and 3 months after adenotonsillectomy.

Results: Post-adenotonsillectomy, the oropharyngeal level neck thickness significantly increased in all children (49.2 ± 11.3 to 60.0 ± 8.4 mm; $p<0.05$). The lateral pharyngeal wall thickness significantly decreased under Müller maneuver (from 26.1 ± 4.4 to 24.1 ± 3.7 mm; $p < 0.05$); similarly, its change during the maneuver decreased (from 3.0 ± 1.9 to 1.4 ± 1.4 mm; $p < 0.05$) as well as the change in the parapharyngeal neck thickness (from 8.1 ± 4.7 to 5.8 ± 3.5 mm; $p < 0.05$). However, the lateral pharyngeal wall change was only significant in children without residual obstructive sleep apnea (from 3.8 ± 2.2 to 1.3 ± 1.6 mm; $p < 0.05$). No associations emerged between ultrasonographic parameters and post-operative residual obstructive sleep apnea.

Conclusion: Ultrasonographic measurements revealed increased neck thickness at the oropharyngeal level related to adenotonsillectomy. However, the lateral pharyngeal wall thickness during the Müller maneuver and collapsibility of the upper airway structures decreased in children with obstructive sleep apnea. Nonetheless, no upper airway structure ultrasonographic parameters could independently predict surgical outcomes in patients with obstructive sleep apnea.

S3 L5

Transoral videolaryngoscopic surgery as a minimally invasive treatment for pyriform sinus fistula.

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Pyriform sinus fistula (PSF) is a rare branchial anomaly associated with recurrent cervical infections. Although open neck surgery and endoscopic/microlaryngoscopic ablation/closure are well-known definitive treatments for PSF, the recurrence rate and skin scarring have been a concern. Transoral videolaryngoscopic surgery (TOVS) is a minimally invasive, non-robotic endoscopic surgery for localized early stage laryngopharyngeal cancer. Here, we present a novel transoral surgical technique for PSF using the TOVS and elucidate its efficacy and potential complications.

The surgical procedure was performed under general anesthesia. The apex of the pyriform sinus was expanded using an FK-WO retractor, and the PSF was stained with a blue liquid. The mucosa around the PSF was incised with electric cautery. After peeling off and removing the PSF, the remaining proximal mucosa was sutured to ensure complete closure of the infection route. A retrospective chart review was performed on 11 patients (aged 3–70 years eight females, three males) who underwent this novel procedure for PSF from 2013–2023.

The mean operative time was approximately 116 minutes. Oral intake was initiated approximately three days postoperatively, and the average postoperative hospitalization was approximately eight days. No major complications were observed in any of the 11 patients, except for mild arytenoid edema and swelling of the anterior neck three weeks postoperatively. As of March 2025, there have been no recurrences in any of the cases.

TOVS is a minimally invasive treatment for PSF that appears to be safe, simple, and reliable.

S3 L6

SmartHear+SmartTalk- AI empowering solutions for speech and hearing

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SmartHear is a portable, objective hearing assessment tool developed over ten years, achieving potentially over 95% accuracy. Designed by a team led by Professors Chen Shixiong and Michael Tong, its patented technology is transferable from institutions such as SIAT, CUHK, and CUHKSZ in Greater Bay Area of China. Enhanced with AI algorithms, SmartHear extends its applications beyond traditional clinical settings. Its lower production costs offer two advantages: replacing existing clinical devices with a cost-effective solution and lowering market entry barriers for new businesses.

By analyzing data from various centers, SmartHear refines its AI, ensuring it remains a leader in hearing assessment technology. The integration with other automated hearing tests creates a comprehensive solution that streamlines diagnostics, fitting, and outcome assessments, effectively addressing fragmented patient pathways. Collaborative development with hearing aid and implant manufacturers further solidifies its position in the market.

SmartTalk utilizes Automated Speech Recognition (ASR) technologies, developed since 2016 by Cymie Ng, Michael Tong, and Tan Lee at CUHK, with government and NGO support. This tool is particularly effective in early childhood education, such as kindergartens. Recent advancements, including coupling ASR with large language models, enhance its user interface. SmartTalk improves speech therapists' productivity by automating assessments and managing larger caseloads while providing an integrated platform for parents and teachers to address speech disorders.

Both SmartHear and SmartTalk are endorsed by industrial partners in the hearing implant industry, positioning them as cutting-edge solutions in their respective fields.

S3 L7

An evaluation of an innovation and medical device for treatment of patients suffering from common outer ear and nose problems.

Petri Olivius

Background

Some patients have problems when administering and dosing ear drops and ointment into the ear and the nose.

An evaluation of an innovative instrument was performed as a two-parts study.

Materials and Methods

A descriptive interview was performed during 5 days on 22 patients (15 to 80 years of age) suffering from common outer ear problems (eczema, wax, hearing aid discomfort; n=11) and nose problems (allergy, congestion, nose infection; n=11). The interviews lasted about 5 minutes.

Study nurses were given individual instructions on the instrument which they applied in the ear, nose and eye on patient mannequins. They were exposed to 28 questions and the answers were ranging from 1 (do not agree) to 5 (fully agree).

Results

Out of patients who received spray or drop treatment into the ear or nose some had problems applying the drops. Others used cotton swabs for application of ointment to the nose.

For the nurses most were positive to the instrument and found it intuitive and easy to use.

The total summarized result from usage of the instrument in ear, nose and eye for all nurses was 4,25± 0,49 (mean ± standard deviation).

Conclusion

Dosing drugs and ointment into the ear and nose may be challenging. Here, as evaluated by the study nurses in this study, Doseen® may be useful due to its safe and simple design. Furthermore, if the instrument is used to lubricate patients with simple itching problems in the ear canal further usage of cotton swabs may be reduced.

S3 L8

Novel Chd7+/CreERT2 and Chd7FAST/+ mice for exploring cell lineage and overexpression as preclinical studies for gene therapy in CHARGE syndrome

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Deafblindness in humans is often caused by loss or disruption of a single gene, as in Usher or CHARGE syndromes. This underlying mechanism (known as haploinsufficiency) may be amenable to gene therapies that upregulate the remaining normal allele, as was shown for Sim1-mediated obesity in mice. We are performing pre-clinical studies of Chd7 haploinsufficiency in mice to identify which cellular lineages in the ear require Chd7 for proper function, and to determine whether increased Chd7 expression has therapeutic or detrimental effects. Toward this end, we developed two novel Chd7 mouse lines: Chd7+/CreERT2 knockin mice to test the timing, specificity, and maintenance requirements for Chd7 and Chd7FAST/+ mice which enable overexpression of Chd7 in a time- and tissue-specific manner. Chd7CreERT2/+ and Chd7FAST/+ mice exhibit circling behaviors suggesting Chd7 haploinsufficiency. We confirmed null status using anti-CHD7 staining in e10.5 homozygous embryos. Lineage tracing with Cre reporter activity and Tamoxifen exposure showed Chd7-Cre+ cells form as early as e8.5, at the onset of otic placode formation. Chd7-Cre+ cells are abundant in the e12.5-e14.5 cochleovestibular ganglion (CVG) and inner ear sensory epithelia. Temporal deletion of Chd7 in Chd7Flox/CreERT2 embryos identified a critical window for Chd7 in formation of vestibular structures. These studies demonstrate that Chd7+/CreERT2 mice faithfully express Cre from the Chd7 promoter and are a useful tool for determining the contributions of CHD7 to inner ear development and function. These preclinical studies will contribute to gene therapy approaches that may help treat CHARGE and related causes of deafblindness.

S3 L10

Real-time navigation surgery for parathyroid adenoma using projection mapping with indocyanine green fluorescence

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Background

Surgical resection is indicated for hyperfunctioning parathyroid glands, making reliable intraoperative identification essential. However, identifying the glands during surgery can be challenging, particularly when preoperative imaging fails to detect them due to lack of enlargement, or when anatomical variations—especially in the lower glands—are present.

Materials and Methods

We utilized a real-time navigation system developed at Kyoto University that employs projection mapping with indocyanine green (ICG) fluorescence to assist in the identification of parathyroid adenomas. Sixteen patients with parathyroid adenoma who underwent surgery between April 2021 and July 2024 were included in this study.

Results

The parathyroid glands were successfully identified in all cases using this system. Unlike conventional near-infrared fluorescence imaging systems, which require viewing the fluorescence signal on a monitor in a dark room, this system projects the fluorescence signal directly onto the surgical field in real time using projection mapping technology, thereby enhancing visibility and facilitating intraoperative identification.

Conclusion

The real-time navigation system with projection mapping using ICG fluorescence enabled clear identification of parathyroid adenomas. While further improvements are needed—such as enhancing excitation light intensity and detection sensitivity—our findings demonstrate the potential utility of this system in the surgical identification of parathyroid adenomas.

S3 L11

Treatment with Mesenchymal Stem Cells for Xerostomia – a systematic review and meta-analysis

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Background:

Xerostomia leads to debilitating oral symptoms 24/7. Two of the most frequent causes of xerostomia are radiotherapy in the head and neck and Sjögrens disease. Only symptomatic treatment is available today. An increasing number of studies have suggested that mesenchymal stem cell (MSC) transplantation treatment can increase the salivary flow rate and ameliorate symptoms of xerostomia. The primary outcome of this meta-analysis is the change in the unstimulated salivary flow rate (UWS) after MSC treatment.

Methods:

The databases MEDLINE, EMBASE, and Cochrane was searched for eligible studies. Inclusion criteria: clinical trials including patients with xerostomia due to either radiotherapy or Sjögrens disease and who were subsequently treated with MSC. Risk of bias was assessed. A meta-analysis was conducted using a random effects model. The protocol was published a priori.

Results:

5 trials were included. All patients received treatment with intraglandular injections in the salivary glands. In the meta-analysis the median difference increased by 0.35 ml/min or approximately 30% (95%CI: -1.12ml/min to 1.83 ml/min) in UWS favoring MSC treatment. No treatment related serious adverse events (SAE) were observed. Minor, temporary treatment related adverse events were observed.

Conclusion:

This is the first meta-analysis evaluating MSC treatment for xerostomia in human clinical trials. A non-significant increase in UWS was observed. Further, no SAEs were observed supporting current evidence that MSC treatment is safe. Further studies are needed to evaluate the observed increases in UWS, e.g. in a phase III trial for radiation-induced xerostomia and in a phase II trial for Sjögren-induced xerostomia.

S3 L12

Recurrent Laryngeal Papillomatosis in Denmark from 1994 to 2021: A Nationwide Register Study

Preben Homøe, Ulrik Steen Nielsen Nielsen, Eva Rye Rasmussen, Andreas Jørkov

Objectives: The aim of this study is to describe the incidence and demographics of laryngeal papillomatosis (LP) in Denmark, including sex and age distribution, recurrence rates, and HPV subtypes, using a new method of register identification.

Methods: The data were extracted from the Danish Pathology Data Bank using SNOMED codes instead of the usual method using ICD codes from the Danish National Health Register. The derived pathology records were manually verified by three medical doctors. The study period was 1994 -2021. Patients were categorized according to age as either juvenile-onset RRP (JoRRP) if <18 years or adult-onset RRP (AoRRP) if 18 years or older.

Results: We identified 1819 RRP patients (JoRRP: 56; AoRRP:1763). The overall incidence per 100,000 inhabitants were 0.17 for JoRRP and 1.45 for AoRRP. The vast majority (72%) of the patients were male, but there was no significant difference in age at onset of RRP or recurrence rates between the sexes. Children below 3 years of age had the highest recurrence probability. Extracting data using SNOMED codes resulted in a positive predictive value of 99% regarding total number of biopsies and 98% regarding individuals. The incidence decreased throughout the study period.

Conclusion: Comparable incidence and recurrence rates of RRP were found between Denmark and Norway. In this study, the Danish Pathology Register was found to be a highly valuable method for identifying LP patients. The effect of the nationwide HPV vaccination program can be evaluated using this method as the vaccinated cohort is starting to grow older and reproduce.

S3 L13

METABOLOMICS ANALYSIS OF PLASMATIC MARKERS IN PEDIATRIC PATIENTS AFFECTED BY OSA WITH AND WITHOUT OTITIS MEDIA

Nicola Quaranta, Framncesco Salonna, Nicoletta Lionetti, Maria Grazia Di Lago, Nicola Quaranta

Background

Obstructive Sleep Apnea Syndrome (OSAS) in the pediatric population is a relatively common condition associated with impaired growth and development. Conductive hearing loss can occasionally complicate pediatric OSAS, although the pathophysiological basis of this association remains unclear. The present metabolomic study aims to compare the amino acid and acylcarnitine profiles between pediatric patients with isolated OSAS and pediatric patients with OSAS complicated by conductive hearing loss, in order to identify potential biomarkers and better understand underlying metabolic mechanisms.

Materials and Methods

A prospective metabolomic study was conducted on two groups of pediatric patients: the first consisting of 11 patients diagnosed with OSAS confirmed by polysomnography (PSG), and the second of 10 patients diagnosed with both OSAS (confirmed by polysomnography) and conductive hearing loss (diagnosed by audiological examinations).

Results

Comparative statistical analysis of the metabolomic profiles revealed significant differences in the levels of specific amino acids (cysteine, GABA, homoalanine, and hydroxylysine) and acylcarnitines (C2, C5, and C8:1) in both groups compared to reference values. Furthermore, the group with OSAS and conductive hearing loss showed alterations in additional amino acids and acylcarnitines compared to the OSAS-only group (Fig 1 and 2).

Conclusions

Metabolomic analysis showed significant difference in OSAS patients in amynoacids and acylarnitines. This molecules may be used as circulating biomarkers and/or nutraceutical targets.

S3 L14

Potential for prevention of dementia in Japan

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Background

In 2017, Livingstone et al. reported in the Lancet Commission Report that among the modifiable risk factors for dementia, hearing loss in midlife and later years had the greatest potential contribution to dementia prevention. The estimated contribution of hearing loss has changed from 9% in the 2017 report to 8% in the 2020 report and 7% in the 2024 report; however, it remains the most significant factor.

Since the prevalence of risk factors for dementia, including hearing loss, varies significantly across countries, their respective contributions to dementia onset are also expected to differ. Therefore, calculating the contribution of hearing loss in each country is essential for policymaking and public health initiatives.

Materials and Methods

In this study, we investigated the contribution of hearing loss to dementia incidence in Japan through a collaborative research project with the Danish Dementia Research Centre at the University of Copenhagen and the Kingdom of Denmark.

Results

Our findings suggest that 39% of dementia cases in Japan may be potentially modifiable. Among these, hearing loss from midlife to later life was the most significant factor, contributing 7%, followed by physical inactivity at 6%, and high LDL cholesterol at 4%.

Conclusion

Our research clearly demonstrates that hearing loss, as with global findings, represents the most impactful and actionable target for intervention in Japan.

S3 L15

Revisiting the Hypoglossal-Facial Nerve Transfer for Facial Reanimation in 2025? The renaissance of an old technique.

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The most commonly used donor nerves for facial reinnervation include the masseter, hypoglossal, and contralateral facial nerves. While the classical hypoglossal-to-facial (HTF) nerve transfer—requiring complete transection of the XII nerve—has declined due to associated morbidity, a renewed interest in HTF has emerged.

Several key factors have contributed to this resurgence. First, partial HTF techniques that reroute the intratemporal segment of the facial nerve without the need for a nerve graft now yield comparable or superior outcomes to the classical method, while preserving tongue function in over 90 percent of cases.

Second, dual nerve transfers have gained popularity. Patients undergoing masseter-to-facial or cross-face nerve grafts often experience insufficient static facial tone. Combining these with HTF provides both spontaneous and powerful input, improving overall facial symmetry and dynamic motion compared to single transfers.

Third, in cases where skull base procedures are required and the facial nerve is already compromised, HTF can serve as a proactive strategy. It effectively bypasses the damaged facial nerve, allowing safe tumor resection while simultaneously delivering a robust motor source for reanimation.

These advances have elevated the role of HTF in comprehensive facial reanimation strategies within specialized facial palsy units. This presentation will highlight practical surgical techniques and include illustrative case examples and videos to support each of these evolving indications.

S3 L16

Evaluation of Sound-Based Sleep Stage Prediction in Shared Sleeping Settings

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[1] Seoul National University College of Medicine, Seoul National University Bundang Hospital, [2] Asleep

Background/Objective: Sound-based AI models for sleep staging face challenges in shared sleeping environments due to acoustic interference from bed partners. This study aimed to evaluate the performance of a sound-based model in two-person polysomnography (PSG) scenarios, with independently recorded sound data for each participant.

Methods: Eighty-eight participants (37 males, 51 females) were recruited, including 74 from mixed-gender pairs and 14 from all-female pairs. Bed partners underwent simultaneous PSG in a shared room, with sound recorded separately for each participant using MEMS microphones placed 1.2 meters from the bed, oriented toward the closest participant. Sleep staging was classified into 4-stage (wake, REM, light NREM, deep NREM), 3-stage (wake, REM, NREM), and 2-stage (wake, sleep) categories. Macro F1 scores were used to evaluate the model's performance.

Results: The model achieved macro F1 scores of 0.629, 0.696, and 0.768 for 4-stage, 3-stage, and 2-stage classifications, respectively. Performance for 4-stage classification varied by group composition, with scores of 0.620 for mixed-gender pairs and 0.670 for all-female pairs. Subgroup analyses revealed higher scores for males (0.710) compared to females (0.565) and for individuals with higher BMI (0.707), higher AHI (0.702), and higher sleep efficiency (0.671).

Conclusion: This study demonstrates the ability of a sound-based model to predict sleep stages effectively in shared sleeping environments, overcoming the interference challenges from bed partners. Future research will aim to refine the model for broader demographic applicability.

S3 L17

How to grow old healthy

jukka ylikoski, Timo Poijärvi, Kuu Ikäheimo

Ageing is characterized by a gradual loss of energy leading to loss of normal physiological function, culminating in frailty and increased susceptibility to a variety diseases. The main source of energy is the oxygen in the air we breathe, which is carried to our body by our bloodstream. Both lung function and the efficacy of vascular supply of organs decline with age by 1-2% per year from the age of 25. Therefore, perhaps the most important cause of aging and related diseases is an imbalance between energy intake and demand. Therefore, aging and hypoxia can be equated. Even mild hypoxia can lead to oxidative stress (OS), which is the underlying cause of most neurodegenerative diseases, including age-related hearing loss (ARHL). Middle-aged ARHL is by far the greatest risk factor for Alzheimer's disease. The targeted treatment for OS is oxygen. Hypoxia has been successfully treated for over 60 years with hyperbaric oxygen therapy (HBOT) and several preclinical studies have shown that age-related neurodegenerative diseases, including Alzheimer´s disease can be successfully treated with HBOT. In addition, a research team was recently able to reverse the aging process by 25 years using HBOT.

In addition to OS, aging also brings with it other stresses which facilitate chronic low-grade inflammation. The combination of stress, hypoxia, and inflammation are associated with chronic sympathetic hyperactivity. The specific treatment for this is to increase parasympathetic or vagal activity. This is best done with transcutaneous vagal stimulation (taVNS). taVNS has been shown to be a simple and effective tool that promotes healthy aging. All this suggests that two strategies to prevent/slow down age-related dysfunctions and diseases are to correct hypoxia and reduce stress.

S3 L18

In vivo regeneration of rat laryngeal cartilage with mesenchymal stem cells derived from human induced pluripotent stem cells via neural crest cells

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Background

Laryngotracheal cartilage plays a critical role in maintaining airway structure, yet it has limited regenerative capacity. While mesenchymal stem cells (MSCs) have been investigated for cartilage repair, autologous MSCs are limited by donor variability and reduced proliferative capacity. Human-induced pluripotent stem cell-derived MSCs (iMSCs) offer an alternative with unlimited expansion potential. We aimed to evaluate the regenerative potential of iMSCs derived via neural crest cells (NCCs) for thyroid cartilage regeneration.

Materials and Methods

Human iPSCs were differentiated into iMSCs through NCC intermediates under xeno-free and serum-free conditions. Then, clumps fabricated from an iMSC/extracellular matrix complex (C-iMSC) were transplanted into thyroid cartilage defects in immunodeficient (X-SCID) rats. Histological and immunohistochemical analyses were conducted at 4 and 8 weeks postoperatively to evaluate cartilage regeneration and cell survival.

Results

C-iMSCs survived and integrated into the defect sites, as confirmed by human nuclear antigen (HNA) staining. Cartilage-like tissue formation with lacunae was observed, and transplanted cells co-expressed SOX9, a chondrogenic marker. Type II collagen, a hallmark of hyaline cartilage, was detected around HNA-positive cells, while type I collagen was absent. Regenerated tissue was contiguous with native cartilage. Cartilage-like regeneration was observed in 71% of transplanted rats.

Conclusion

iMSCs derived from human iPSCs via NCCs promoted cartilage regeneration in vivo and partially differentiated into chondrogenic cells. The use of xeno-/serum-free culture conditions enhances clinical relevance. These findings support iMSCs as a promising cell source for future laryngotracheal reconstruction therapies.

S3 L19

Genetic analysis of carotid body tumors: preliminary findings

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Background

Carotid body tumors (CBTs) are rare tumors arising at the bifurcation of the carotid artery and are pathologically classified as paragangliomas. Germline genetic alterations—particularly in succinate dehydrogenase (SDH) subunit genes—are known to be involved in their development. However, the mechanism of tumor progression remains unclear.

Materials and Methods

Whole-genome sequencing and RNA sequencing were performed on surgical specimens from six cases of CBT to investigate gene expression profiles. CBT expression data were compared with those from normal tissues and pheochromocytomas/paragangliomas (PCPG) using publicly available data from The Cancer Genome Atlas.

Results

Germline variants in SDHx genes were identified in five of the six cases. The expression levels of all four SDH subunit genes were lower in CBTs compared with normal tissues and PCPG. A comprehensive analysis using single-sample Gene Set Enrichment Analysis (ssGSEA) revealed no significant differences in proliferative activity among the samples. However, notable differences were observed in the activity of immune-related pathways, with one tumor showing higher activation of multiple immune pathways compared to the others.

Conclusion

Although this study involved only a small number of cases, the results suggest that the downregulation of SDH-related genes plays a key role in CBT pathogenesis. Furthermore, the findings imply that individual CBTs may exhibit distinct immune profiles, highlighting a possible strategy for personalized therapeutic approaches.

S4 L1

Therapeutic Potential of Ginsenoside Rb2 as a TMEM16A Potentiator in Cystic Fibrosis Sinusitis

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Background: Cystic fibrosis (CF) is marked by defective chloride (Cl^-) secretion due to CFTR dysfunction, leading to thick mucus and impaired mucociliary clearance (MCC). While CFTR modulators benefit many patients, mutation-independent therapies are needed. Our prior studies showed Korean Red Ginseng aqueous extract (RGAE) improves MCC via TMEM16A potentiation. This study evaluates individual ginsenosides, focusing on ginsenoside Rb2, as TMEM16A potentiators for restoring Cl^- transport in CF sinus and lung disease.

Materials and Methods: $CFTR^{-/-}$ rat nasal epithelial cultures were used to assess Cl^- transport through Ussing chamber analysis after ginsenoside treatment. The three most promising ginsenosides (Rb2, Rd, Rg3s) were further evaluated in TMEM16A-transfected HEK293 cells using whole-cell patch clamp. Cytotoxicity was assessed by LDH assay, and intracellular calcium changes were monitored using Fluo-4 AM dye.

Results: All tested ginsenosides significantly activated TMEM16A-mediated Cl^- transport, with Rb2 eliciting a strong ΔIsc ($82.8 \pm 7.2\ \mu A/cm^2$, $p<0.0001$). In patch clamp analysis, Rb2 was the most potent activator (870.1 ± 344.4 pA, $p<0.05$). Rb2 did not increase cytosolic calcium or show cytotoxic effects. These in vitro results align with prior in vivo studies showing that RGAE improved nasal potential difference, mucociliary transport, and histopathology in $CFTR^{-/-}$ rats.

Conclusion: Ginsenoside Rb2 is a potent and safe TMEM16A potentiator that restores Cl^- secretion independent of CFTR and calcium signaling. This lead compound for TMEM16A-targeted therapy offers a novel mutation-agnostic approach to restore airway hydration and mucociliary function in CF sinusitis. Preclinical studies are underway to evaluate Rb2 in Pseudomonas-infected CF rats.

S4 L2

The MACRO Trial: A Randomised Controlled Trial of Clarithromycin and Endoscopic Sinus Surgery for Adults with Chronic Rhinosinusitis with and without nasal polyps

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Background: Evidence regarding use of antibiotics and endoscopic sinus surgery (ESS) in managing chronic rhinosinusitis (CRS) is lacking. The trial objective was to compare clinical-effectiveness of adding ESS or prolonged clarithromycin to intranasal medication (IM) in adults with CRS with (CRSwNP) or without nasal polyps (CRSsNP).

Methods: A 3-arm randomised controlled trial recruited at 20 UK sites. CRS patients remaining symptomatic after receiving IM comprising corticosteroids and saline irrigations were randomised 1:1:1 to receive ongoing IM plus either 1) ESS, 2) clarithromycin (250mg bd for 2 weeks then od for 10 weeks) or 3) matched placebo. Participants and medical staff were blinded to medical interventions but not surgery. Primary outcome measure was the SNOT-22 disease-specific quality-of-life (QOL) questionnaire at 6 months. Secondary outcomes included generic QOL and cost-effectiveness. An intention-to-treat analysis was undertaken. ISRCTN: 36962030.

Results: 181/514 (35.2%) female and 333/514 (64.8%) male participants, with CRSwNP (n=410) or CRSsNP (n=104), were recruited between 2018 -2023 and randomised to ESS (n=171), clarithromycin (n=172), or placebo (n=171). Statistically significant mean differences in SNOT-22 favoured ESS over the other groups (-18.13, (98.33%,CI -24.26, -11.99) and -20.44, (98.33%,CI -26.42, -14.46), respectively), secondary outcomes showed significantly greater improvements with surgery versus clarithromycin or placebo. No significant benefit of clarithromycin over placebo was found.

Conclusion:

ESS improves disease-specific QOL at 6 months in CRS patients. There is no evidence supporting the routine use of low-dose clarithromycin in CRSwNP while benefit in CRSsNP remains uncertain.

S4 L3

Real-world effectiveness of dupilumab in a European cohort of chronic rhinosinusitis with nasal polyps (CHRINOSOR)
Claus Bachert

Pivotal studies with dupilumab demonstrated clinically relevant improvements in nasal polyp score, symptom score, and quality-of-life score in patients with chronic rhinosinusitis with nasal polyps (CRSwNP). We evaluated the effectiveness of dupilumab in a large-scale CRSwNP cohort from 6 European tertiary-care centers. Nasal polyp score, Sinonasal Outcome Test 22 score, visual analog scale for total sinus symptoms, loss of smell, and nasal blockage, and Asthma Control Test score were assessed at baseline and after 24 and 52 weeks' treatment with Dupilumab. Treatment effectiveness was evaluated in relation to demographic and lifestyle factors, sinus surgery history, presence of comorbidities, and blood eosinophil counts (BEC). Treatment response was evaluated according to European Forum for Research and Education in Allergy and Airway Diseases (EUFOREA) 2021 criteria.

All patient outcomes improved at 24 and 52 weeks' treatment compared to baseline. Dupilumab showed effectiveness independent of age, BMI, smoking status, prior sinus surgery, asthma, NSAID–exacerbated respiratory disease, allergy, or baseline BEC. A total of 92.5% and 94.4% showed an improvement in at least 1 EUFOREA criterion at 24 and 52 weeks, respectively; 54.4% and 68.2% met all 4 criteria at 24 and 52 weeks, respectively. Conclusions: Real-world evaluation of dupilumab effectiveness demonstrates a robust and sustained response in at least two thirds of patients at 52 weeks' treatment. Favorable treatment response was independent of the number of surgical procedures, comorbidities, or baseline levels of inflammation.

S4 L4

ASA Treatment in CRSwNP Patients with NSAID exacerbated respiratory disease: Results from a Randomized Double-Blind Clinical Study

Sanna Toppila-Salmi, Alma Helevä

Non-steroidal anti-inflammatory drug-exacerbated respiratory disease (N-ERD) is a chronic inflammatory disorder characterized by sensitivity to NSAIDs, asthma, and/or chronic rhinosinusitis with nasal polyps (CRSwNP). Individuals with N-ERD are at increased risk for severe hypersensitivity reactions, repeated sinonasal surgeries, and reliance on systemic corticosteroids. Aspirin treatment following desensitization (ATAD) is one therapeutic approach for managing N-ERD. The desensitization process involves gradually increasing doses of aspirin over several days, followed by long-term maintenance therapy. This study aimed to assess the effectiveness of ATAD in adult CRSwNP patients with asthma and N-ERD.

A total of 41 adult patients with CRSwNP, asthma, and confirmed N-ERD participated in this randomized, double-blind clinical trial. Of these, 26 successfully completed aspirin desensitization and were randomized to receive either placebo or 250 mg of aspirin daily for 11 months. Outcome measures included the Sinonasal Outcome Test-22 (SNOT-22), nasal polyp score (NPS), Asthma Control Test (ACT), and the EPOS 2012 clinical control assessment for CRS. These were evaluated at four follow-up visits conducted at 1, 5, 11, and 12 months post-treatment initiation.

Linear mixed effects modeling revealed no statistically significant differences between the placebo and aspirin groups over time for SNOT-22 ($p = 0.17$), ACT ($p = 0.45$), or NPS ($p = 0.18$). Additionally, neither group showed meaningful improvement in CRS control according to EPOS 2012 criteria.

Taken together, there was no significant clinical difference between ATAD and placebo in the treatment of CRSwNP patients with asthma and N-ERD.

S5 L1

Neurotrophin Gene Therapy using Bionic array Directed Gene Electrotransfer (BaDGE) of Naked DNA Encoding BDNF and NT -3 Improves Cochlear Implant Hearing Outcomes

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Background: The Cochlear Implant Neurotrophin Gene Therapy (CINGT) (www.cingt.info) study is a phase I /IIa first-in-human clinical trial to evaluate the safety and efficacy of neurotrophin gene augmentation during cochlear implant surgery to 'close the neural gap'. The study followed preclinical workup of naked neurotrophin gene electrotransfer (GET) cochlear nerve regeneration (Pinyon et al. 2024 Adv. Sci. doi:10.1002/advs.202401392).

Materials and Methods: The BaDGE electro-lens was developed from the Cochlear CI522 array, with current pulse-based delivery of pFAR4 miniplasmid DNA encoding brain-derived neurotrophic factor (BDNF) and neurotrophin-3 (NT-3). The procedure was followed by CI622 implantation. Design: CINGT group (17 subjects; severe-profound hearing loss; 27-79 years); 8 Controls. Safety was assessed using impedance and monitoring of adverse events.Hearing outcome measures included: Psychoacoustic bipolar and monopolar threshold (T) and comfort (C) levels, speech perception tests, and electrical auditory brainstem response (eABR).

Results: An excellent safety profile was achieved, with no reported adverse reactions and normative impedance data out to 12 months. There was a significant location-dependent reduction in bipolar T-levels and dynamic-range in the mid–apical cochlear region, mapping to the place-specific GET, which was absent in the Control group. The CINGT group showed rapid rehabilitation in speech tests (CUNY & CNC). eABR demonstrated significant reduction in wave V latencies in CINGT vs. Control groups (combined visits up to 3 months).

Conclusion: The CINGT clinical trial showed the benefit of site-directed neurotrophin gene augmentation in cochlear implant surgery with both behavioural and objective electrophysiological measures of improved hearing outcomes.

S5 L2

A novel delivery procedure for inner ear gene therapy.
Barbara Canlon

Experimental inner ear gene therapy can effectively restore hearing in neonatal mice, but it is complicated in adulthood by the structural inaccessibility of the cochlea. The development of alternative delivery routes may advance inner ear gene therapy and also prove useful when translated to humans with hearing loss. Cerebrospinal fluid flow via the glymphatic system is emerging as a new approach for brain-wide drug delivery in rodents as well as humans. The cerebrospinal fluid and the fluid of the inner ear are connected via the cochlear aqueduct, but previous studies have not explored the possibility of delivering gene therapy via the cerebrospinal fluid to restore hearing in adult deaf mice. Here, we showed that the cochlear aqueduct in mice exhibits lymphatic-like characteristics. In vivo timelapse magnetic resonance imaging, computed tomography, and optical fluorescence microscopy showed that large-particle tracers injected into the cerebrospinal fluid reached the inner ear by dispersive transport via the cochlear aqueduct in adult mice. A single cisternae magna injection of adeno-associated virus Slc17A8, which encodes vesicular glutamate transporter-3 (VGLUT3), rescued hearing in adult deaf Slc17A8−/− mice by restoring VGLUT3 protein expression in inner hair cells. Our findings demonstrate that cerebrospinal fluid transport comprises an accessible route for gene delivery to the adult inner ear and may represent an important step toward using gene therapy to restore hearing in humans.

S5 L3

Gene transfer of transcription factors induces hair cell regeneration in mature mammalian cochleae

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Background:

A combination of transcription factors (TFs) that play a role in hair cell (HC) development is also able to bestow a HC phenotype on other types of cells in culture (Costa et al., 2015, Menendez et al., 2020).

Materials and Methods:

We tested a similar TF cocktail, Gfi1, Atoh1, Pou4f3, with or without Six1 (GAP or GAPS) in mature animals in vivo, for its ability to induce HC regeneration. We used the Pou4f3-DTR mouse, where an injection of diphtheria toxin (DT) leads to degeneration of all cochlear HCs leaving behind supporting cells (SCs). DTR mice were deafened by injecting DT (25 ng/g). Adenovirus vectors containing gene inserts for GAP or GAPS were injected into the endolymph. The contralateral ear served as a control. One month later, cochlear whole-mounts were analyzed for presence of Myosin VIIa+ cells using epi-fluorescence or confocal microscopy.

Results:

Both groups (GAPS and GAP) exhibited HCLCs in the experimental (left) ear. GAPS group animals included 4 out of 10 animals with a large number of HCLCs. In the GAP group, 5 out of 10 animals had a large number of HCLCs. In both groups, HCLCs were located within the auditory epithelium and in ectopic locations.

Conclusions:

GAP cocktail of TF transgenes appears to convert SCs to HCLCs in a similar way to the GAPS vector. The next important step is to transition the work to the AAV platform which is less toxic and more applicable for human clinical use.

S5 L5

Surgical procedure for injection of cells and substances into the human cochlear modiolus

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BACKGROUND

Partial restoration of hearing can be achieved by direct electric stimulation of spiral ganglion neurons (SGNs) using a cochlear implant (CI). However, effectiveness of a CI depends on the presence and functionality of SGNs and the auditory nerve, implying that individuals with limited or absent SGNs will not benefit fully from an implant. Currently, this subgroup of existing CI users and potential CI candidates find themselves devoid of alternative options, apart from a brain stem implant.

MATERIAL AND METHODS

With the perspective of gene therapy or injection of e.g. stem cells and/or neurotrophic substances into the modiolus, we demonstrate the feasibility and accuracy of a minimally invasive surgical access to the modiolus via the external auditory canal, using ten human temporal bones. Upon opening the modiolus, glass or metal microbeads were injected into the modiolus using a mechanical system for steady and volume-controlled injection. The surgical access route, precision and volume of the injected material were evaluated using μCT and histology, followed by 3D reconstruction of the cochleae.

RESULTS

Cell-sized beads can be accurately targeted to the human modiolus, with minimal tissue damage, low variability and containment of the injected volume within the modiolus. The approach is compatible with an already implanted CI electrode array, suggesting applicability to both existing and future CI users.

CONCLUSION

We hereby demonstrate the feasibility and precision of a minimally invasive, transcanal surgical approach to the modiolus of the human cochlea, paving the way for future local delivery of gene, cell or substance therapy.

S6 L1

A blood barrier on a chip model gives no insights into Meniere's disease

Daniel Bidmer, Mirijana Sekuiic, Vesna Petkovic

Background

Meniere`s disease is a disorder of the vestibular system and includes episodic vertigo, aural fullness, tinnitus and fluctuating hearing loss. The disease has been first described by Prosper Meniere in 1860, however, its exact pathophysiology remains elusive. A key histopathological feature is the buildup of endolymphatic fluid within the membranous labyrinth of the inner ear, called the endolymphatic hydrops. Today, several theories are discussed to explain cochlear vestibular dysfunction related to the endolymphatic hydrops, such as membranous labyrinth rupture, ischemic attack, inflammation and hydraulic pressure fluctuations.

Material and Methods

We developed a microfluidic chip model which mimics the human blood labyrinth barrier. We first investigated how inflammatory factors influence the integrity and function of this blood labyrinth barrier model. Second, we investigated whether blood from Meniere`s disease patients affect the blood labyrinth barrier compared to control patients.

Results

Using our microfluidic chip model, we were able to demonstrate that Neutrophil extracellular traps resulted in a dose-dependent effect on inner ear derived endothelial cells as indicated by a reduced electric resistance transepithelial permeability in our chip model. Most interestingly, serum from Meniere's disease patients resulted also in reduced electric resistance in our model system compared to serum from control patients

Discussion and Conclusion

The blood labyrinth chip model gives the possibility to easily monitor and model the diffusion of substances from the blood to the inner ear. Using this model, we could observe that in Meniere's disease patients the blood-labyrinth barrier is altered.

S6 L2

Superiorly Based Pre-/Postauricular Transposition Flap to Enlarge the External Ear Meatus in Endaural Otologic Surgery

ORHAN OZTURAN, EMRE POLAT, FADLULLAH AKSOY, SABRI BAKI EREN

Background:

Endaural access is widely used in otologic surgery for conditions like chronic otitis media, myringoplasty, and tympanoplasty. However, it may cause disproportionate enlargement of the osseous outer ear canal (OEC) without sufficient widening of the external auditory meatus. This mismatch can lead to infection, conductive hearing loss, and poor aural hygiene. A well-proportioned OEC and meatus are essential for ventilation and self-cleaning. This study evaluates superiorly based preauricular and postauricular transposition flaps for balanced meatal enlargement after endaural surgery.

Materials and Methods:

A retrospective review was conducted on six patients who underwent OEC enlargement via endaural surgery at a tertiary center between August 2023 and April 2025. Preauricular flaps were used for patients over 45 years with redundant pretragal tissue; postauricular flaps were chosen for younger patients or those with firm pretragal skin. Outcomes were assessed by otoscopy, focusing on meatal patency and function.

Results:

All patients achieved successful meatal enlargement with good patency and no major complications. Pedicled flaps promoted minimal scarring, smooth epithelialization, and canal integration. Patients reported improved hygiene and fewer infections.

Conclusion:

Superiorly based preauricular and/or postauricular flaps offer a reliable, simple method for enhancing external auditory meatus size post-endarural surgery. This technique improves aeration, self-cleaning, and reduces complications, with favorable cosmetic and functional outcomes.

S6 L3

Preliminary efficacy and safety of AK-OTOF gene therapy for OTOF-mediated hearing loss

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Background: The otoferlin gene (OTOF) encodes otoferlin, a protein critical for signaling at inner hair cell synapses; individuals with OTOF mutations initially present with congenital, severe to profound sensorineural hearing loss, with preserved otoacoustic emissions. Advances in gene therapy and intracochlear delivery support potential hearing restoration in individuals with OTOF-mediated hearing loss using a one-time, local administration of AK-OTOF (AAVAnc80-hOTOF). This multicenter Phase 1/2 clinical trial (NCT05821959) evaluates the investigational medicinal product, AK-OTOF, and the investigational medical device, the Akouos Delivery Device, used to administer AK-OTOF to the intracochlear space.

Materials and Methods: Eligible participants have profound hearing loss, as assessed by auditory brainstem response (ABR), at baseline and receive, using a minimally invasive transcanal approach, a single intracochlear administration of AK-OTOF in one ear. Safety assessments and hearing restoration, including by ABR and behavioral audiometry testing, are assessed over the one-year trial and an additional four-year long term follow-up period.

Results: The first participant, an 11-year-old, experienced restored hearing within 30 days of AK-OTOF administration; behavioral thresholds were 65 to 20 dB HL. The second participant, an 8-year-old, also experienced restored hearing within 30 days of AK-OTOF administration. The surgical administration and AK-OTOF were well tolerated, and no trial-related serious adverse events have been identified as of the date of this report. Updated safety and efficacy data from these and additional participants will be presented.

Conclusions: Interim data suggest that AK-OTOF may be safely administered to patients with onset of hearing restoration as early as one month following administration.

S6 L4

Gene Delivery to the Inner: Overcoming Challenges and Advancing Therapies using the pig as a large animal model

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Gene therapy has emerged as a promising curative approach for genetic hearing disorders by directly addressing the molecular basis of disease. Over the past two decades, this field has evolved from preclinical work in animal models to successful first-in-human trials. Multiple delivery strategies have been developed to safely and effectively transduce target cells within the inner ear, which we are currently testing in a large animal model.

Adeno-associated viral (AAV) vectors are the most widely used, with various administration routes explored, including round window membrane injection, cochleostomy, stapedotomy, and semicircular canal injection. In our recently established large animal model, the pig, we have tested various approaches using different AAVs (Anc80L65, Php.b, AAV2), and quantified transduction in inner and outer hair cells. Additionally, we analyzed transduction in supporting cells and neurons.

Our results demonstrate variable efficacy in achieving widespread and cell-specific transduction, with several approaches inducing gene expression with minimal trauma and preservation of objective hearing function. These large animal studies further support the feasibility and safety of these delivery methods, while offering valuable data on vector distribution within the inner ear, cell tropism, and immunogenicity.

We observed a variable transduction gradient in inner and outer hair cells along the cochlear axis from base to apex, highlighting the importance of the selected administration route. The absence of a standardized approach remains a major challenge in the field and underscores the need for further comparative studies before widespread clinical translation can be achieved.

S6 L5

Intra- and post-operative experiences from 51 surgeries of a new active transcutaneous bone-anchored implant system – preliminary data of follow-up Dutch patients (N=16) after 24 months

Myrthe Hol

Abstract CORLAS 2025

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Title: Intra- and post-operative experiences from 51 surgeries of a new active transcutaneous bone-anchored implant system – preliminary data of follow-up Dutch patients (N=16) after 24 months

Objective: Sentio (Oticon Medical AB, Sweden) is an active transcutaneous bone-anchored implant system evaluated for safety and performance in a multi-centre, single-arm, prospective, clinical investigation (Clinicaltrials.gov identifier NCT05166265). The objective of this abstract is to focus on intra- and post-operative variables from 51 surgeries, taking place between February 2022 and November 2023. Combined with long-term follow-up (24 months) of the Dutch patients (N=16).

Materials and Methods: The clinical investigation follows individuals with conductive/mixed hearing losses or single sided deafness for a total period of 24-months after receiving an active transcutaneous bone-anchored implant. To date, all 51 included participants have reached primary outcome assessment at 3 months, which is the first timepoint for analysing cohort data. Surgical variables include pre-operative planning, type of anaesthesia, type of surgical incision, and surgery time (first incision to last suture). A postoperative visit, 2 weeks after surgery was done to remove sutures and to assess wound healing, pain, and numbness.

Results: The cohort represents an adult group with a mean age of 50 (range 24-77) years and with a distribution of the type of hearing loss of 51% conductive, 25% mixed, and 24% single sided deafness on the implanted side. Surgery duration is 58 min (range 23 - 85 min) and general anesthesia is used in most cases. Although pre-operative imaging techniques are part of clinical practice in some clinics, more than half of the surgeries was done without it. There was no case of aborted surgery due to insufficient bone thickness and/or unexpected anatomy. The most used incision type was a stepwise C-type (49%), but 'lazy S' type (33%) and other techniques (18%) were also observed. Surgical wounds heal within 2 weeks and the majority of patients report of low levels of pain and numbness. After 24 months all Dutch patients wear the device, no adverse events reported.

Conclusion: This active transcutaneous bone-anchored implant is small and minimal invasive to install. It can safely be implanted without preoperative imaging and surgery time could potentially be optimized to below 30 minutes depending on the individual patient's anatomy and prerequisites. Long-term outcomes are favorable and increase the available options for hearing in alignment with personalized healthcare.

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S6 L6

Health care disparities and genetic hearing loss among the Amish

Marci Lesperance

Background: The Amish are known to have a higher burden of autosomal recessive genetic conditions due to a founder effect. In addition, the Amish are medically underserved, particularly in terms of hearing health care.

Materials and Methods: Audiograms, otolaryngology clinic records, and genetic testing results from an Amish field clinic in Branch County, Michigan.

Results: 33 patients in 11 families have been diagnosed with an inherited form of moderate-to-severe bilateral sensorineural hearing loss (SNHL). Prior to establishing the field clinic, the average age at time of hearing loss diagnosis was 11 years old. Midwives have been trained to screen newborn hearing in the home ana mobile unit with a sound booth has reduced the age of identification.

The incidence of hearing loss is 10-50% in affected sibships and approximately equal sex distribution. Affected parents suggest a founder variant with high carrier frequency. The inheritance pattern is most consistent with autosomal recessive inheritance.

To date, 3 individuals have undergone genetic testing with hearing loss gene panels. One individual was found to have compound heterozygous variants in PEX26 diagnostic of Zellweger spectrum disorder. Two others had negative findings on genetic panel testing. Clinical whole exome sequencing results showed areas of homozygosity on chromosome 10 but did not identify a genetic etiology.

Conclusion: Innovative approaches are necessary to mitigate the barriers to care facing this unique population. The molecular basis of this form of SNHL is largely unknown, and further studies will be necessary to identify the genetic variant(s) segregating in this population.

S6 L7

Otologic manifestations in Achondroplasia

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Background

Achondroplasia, arising from mutations in the FGFR3 gene, is the most common skeletal dysplasia and manifests clinically as marked short stature, craniofacial dysplasia and functional abnormalities. Craniofacial abnormalities may result in various otologic problems, namely recurrent infections and hearing loss. Due to its rarity and variable presentation, knowledge on the spectrum and severity of ENT-related features remain limited.

Subjects and Methods

Retrospective cohort study comprising all patients diagnosed with or treated for achondroplasia at the Helsinki University Hospital in 2000–2023. Patient records were reviewed for ear-related problems, clinical examinations and given treatment.

Results

Cohort comprised 48 patients: 26 (54%) females, median age 31 years (range 13–78). Over half (31, 65%) had prior ear infections, 27 (56%) tympanostomies and of them 44% multiple. Furthermore, 26 (54%) had undergone adenoidectomy and/or tonsillectomy. An audiogram was obtained from 16 (33%) and hearing loss documented in 12 (25%); median age at diagnosis 13 years (range 4–21). All patients with hearing problems had a history of other otologic problems and prior procedure. Hearing deficits were mostly classified as mild; no clear trend on sidedness (10% bilateral) or type (conductive/sensorineural/mixed) was noted. Only two patients had a hearing aid.

Conclusion

Our results indicate a spectrum of otologic problems in achondroplasia, most commonly recurrent infections, tonsil hypertrophy and hearing deficiency. Despite history for decreased hearing and prevalent procedures, few patients were comprehensively examined. Future studies and clinician education on possible ENT-related manifestations of achondroplasia and rare skeletal dysplasias alike is encouraged.

S6 L8

Dynamic cone-beam CT of the middle ear - a novel concept for determining excursion of the ossicles

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Background

Conductive hearing loss can be caused by ossicular chain fixation or discontinuity. Existing methods such as CT imaging and tympanometry can in some cases indicate mobility and/or pathology but cannot quantify the excursion of the ossicles. The aim of this study was to explore dynamic cone-beam CT as a new method for determining the excursion of the ossicles.

Material and methods

Five human cadaveric heads (10 ears) were obtained and clinical CBCT imaging at an isotropic resolution of 0.08 mm was performed. A tympanometer was used to change the pressure of the tympanic membrane midways during the scan. The excursion of the manubrium of malleus and the long process of incus was determined based on manual segmentation of the imaging data.

Results

It was technically possible to perform timed pressurization during CBCT imaging of the middle ear and use 180-degree virtual reconstructions of the negative and positive pressure phases of the scan to quantify the excursion of the malleus and incus. In ears with normal impedance (type-A tympanogram), the average excursion of the manubrium of malleus was 0.61 mm and the long process of incus was 0.27 mm.

Conclusion

The novel concept of dynamic CBCT can be used to determine the excursion of malleus and incus in ears with normal tympanic membrane impedance. This provides additional information over conventional static imaging at atmospheric pressure and other current in vivo methods such as wideband tympanometry. Further studies are ongoing to explore the clinical value of the method.

S6 L9

Imaging of the human inner ear with optical coherence tomography

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Background

The inner ear is small, delicate, and encased within dense bone, making it challenging to image. Hearing loss and vertigo occur when there is an imbalance between the two fluids within it, endolymph and perilymph Here, we translated the technology of optical coherence tomography (OCT) for imaging the human inner ear.

Materials and Methods

We studied three cohorts of patients. Six patients undergoing surgery for chronic otitis media, but who had normal inner ear function, served as controls. Four patients with Ménière's disease undergoing endolymphatic shunt surgery were hypothesized to have endolymphatic hydrops. Nine patients with a vestibular or cochlear schwannoma undergoing translabyrinthine resection were hypothesized to have endolymphatic hydrops. OCT imaging was performed during their procedures using a custom-built device that attaches to a surgical microscope.

Results

Peering through the otic capsule bone, we imaged the lateral and posterior semicircular canals and measured the endolymph-to-perilymph ratio. Compared to controls, patients with Ménière's disease or schwannoma demonstrated endolymphatic hydrops. We assessed the repeatability of this imaging modality for measuring the endolymph-to-perilymph ratio and found that it was highly repeatable. Furthermore, we found that increased endolymph-to-perilymph ratios correlated with the level of hearing loss.

Conclusion

Our findings prove the feasibility of imaging the human inner ear with OCT and demonstrate validity in detecting endolymphatic hydrops. Moreover, this technique permits the accurate measurement of the fluid chambers within the inner ear in real time with adequate sensitivity to guide the management of complex but common ear diseases.

S6 L10

Application of inner ear gene therapy to a Slc26a4 mutant mouse model of fluctuating hearing loss

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Background:

Pendred Syndrome (PS) is one of the most common types of syndromic hearing loss. It is caused by mutations in SLC26A4, which encodes pendrin. Mutations in SLC26A4 have also been shown to cause enlarged vestibular aqueduct (EVA), a common inner ear malformation. Patients with EVA present with fluctuating and progressive hearing loss. In this study, we investigate whether inner ear gene therapy can be used as a treatment for hearing loss in a doxycycline-inducible Slc26a4 mutant mouse model.

Methods:

Adeno-associated virus serotype 8 (AAV8) was used to deliver Slc26a4 cDNA into the inner ears of doxycycline-inducible Slc26a4 mutant mice. The expression of SLC26A4 in this mutant mouse model is controlled by doxycycline administration. It has been shown previously that if doxycycline administration is discontinued on embryonic day 17.5 (DE17.5), these mutant mice exhibit fluctuating hearing loss, similar to patients with EVA. Inner ear gene delivery was performed between P0-P3 using the posterior canal approach. Auditory brainstem response (ABR) was performed to assess hearing fluctuations. Inner ear tissues were processed for confocal imaging.

Results:

The inner ears of DE17.5 mutant mice show minimal pendrin expression. After AAV8-CMV-Slc26a4 treatment, pendrin expression was restored in the spiral prominence, stria vascularis, and endolymphatic sac in DE17.5 mutant mice. The DE17.5 mutant mice also showed reduction in hearing fluctuations compared to non-treated mutant mice.

Conclusions:

Our results suggest that AAV8-CMV-Slc26a4 gene therapy restores pendrin expression and decreases hearing fluctuations in the DE17.5 mutant mice.

S6 L11

The clinical diagnosis of superior canal dehiscence syndrome

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Background:

Superior canal dehiscence syndrome (SCDS) is still a challenging condition in terms of clinical recognition, with delayed diagnosis as a rule. Since the first case series presented in 1998 by Dr Lloyd Minor, the clinical spectrum of SCDS has significantly expanded making the clinical and differential diagnosis of this syndrome more challenging. This is an update on the SCDS diagnostic aspects, from the established diagnostic criteria to the new trends in SCDS clinical testing.

Materials and methods:

I will present and discuss the recently released SCDS diagnostic criteria released by the Barany Society, including the results of the clinical research conducted at our department. Moreover, I will present the new trends in clinical testing of SCDS, which may improve the clinical characterisation of this complex syndrome.

Results and conclusion:

The clinical diagnosis of SCDS is challenging. The recently released international criteria will contribute to the standardization of SCDS diagnosis. However, recent advancements in clinical testing may add new insights in SCDS, representing a possible implementation of the actual diagnostic criteria.

S6 L12

X-linked hearing loss – lessons learnt from long-term follow-up of a rare malformation in a single centre.

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Background: Karolinska is the Swedish referral clinic for all patients that are affected by a temporal bone malformation and require a cochlear implant (CI). One such malformation, X-linked hearing loss, is caused by a mutation of the pou3f4 gene and induces an incomplete partition type three malformation of the cochlea.

Method: Through concentration of these patients to one clinic we have been able to follow the hearing, language and cognitive outcomes after CI in comparison to CI patients with normal cochlea anatomy.

Results: Mutations in pou3f4 were detected in 15 patients in which we described two new point mutations causing a frame-shift mutation. Cochlea implantation was possible, however postoperative electrical stimulation levels were higher as compared with a normal cochlea. Children with IP3 malformation deafness had an atypical outcome with low level of speech recognition (especially in noise), executive functioning deficits, delayed or impaired speech as well as atypical lexical-semantic and pragmatic abilities, and exhibited mental ill-health issues. Electrode deactivation was more common in IP3 malformation, and it was estimated that 25% of electrodes would be deactivated by 15 years of age. Speech perception was correlated to the number of deactivated electrodes.

Conclusion: Through long-term monitoring of this rare malformation in a centralised centre we showed that cochlear implantation is a feasible alternative for children with IP3 malformation deafness. However an extensive and consistent multidisciplinary team approach is required to support their overall habilitation.

S6 L13

Peripheral Blood Cytokine Profiles in Sudden Sensorineural Hearing Loss: Potential Diagnostic and Therapeutic Implications

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Objective: To evaluate the association between peripheral blood cytokine profiles and clinical outcomes in patients with sudden sensorineural hearing loss (SHL) and study

their potential role as diagnostic markers and therapeutic targets.

Materials and Methods: Thirty-two SHL patients and nine non-SNHL patients from 2018 to 2021 were included. Inflammatory cytokine levels were evaluated, including TNF-α, IL-1β, CXCL1, CXCL12, and complement component C5/C5a. Patients were categorized into short-term steroid use (<3 days) and long-term steroid use (4–8 days) groups to evaluate the effect of steroids on cytokine levels. Statistical analyses evaluated the associations between cytokine profiles, initial hearing severity, and treatment outcome.

Results: TNF-α and IL-1β levels were significantly increased in SHL patients compared to controls, while CXCL1, CXCL12, and C5/C5a levels were substantially lower. No significant association existed between cytokine levels and initial hearing severity or treatment outcome. Additionally, TNF-α and IL-1β levels showed no differences between short-term and long-term steroid use groups. However, CXCL1 and CXCL12 levels were significantly decreased in the long-term steroid group.

Conclusions: This study reported the involvement of inflammatory cytokines in SHL, suggesting their potential as diagnostic biomarkers and therapeutic targets. While short-term steroid treatment had no significant effect on cytokine levels, long-term steroid use was associated with decreased CXCL1 and CXCL12 levels, suggesting the need for further investigation. Future studies are needed to evaluate the effectiveness of targeted anti-inflammatory treatments.

S6 L14

The role of CWC27 in cochlear development

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Background

CWC27 is a nuclear cyclophilin protein crucial for pre-mRNA splicing, functioning as part of the activated spliceosome (Bact complex). Mutations in the human CWC27 homolog result in truncated transcripts, causing retinal degeneration, skeletal dysplasia, and developmental abnormalities collectively known as RPSKA. Some patients also experience hearing loss. These conditions are linked to defective mRNA splicing, such as intron retention and exon skipping. Mutant mice with CWC27 deficiency exhibit similar phenotypes, including retinal degeneration due to abnormal mRNA splicing in retinal cells.

Methods

We generated Cwc27 null mice using CRISPR/Cas9 genome editing to investigate its role in auditory development. A stop codon was introduced in exon 1, creating a null allele. We observed the histological morphology of the cochlea using Hematoxylin/Eosin staining.

Results

Homozygous mutant mice displayed embryonic lethality and cranial abnormalities, such as cranium bifida, caused by neural tube defects. The cochlear morphology varied depending on the presence of cranium bifida. Mutant mice with cranium bifida had shorter cochlear ducts (around one turn), while those without it showed one and a half turns. This suggests that CWC27 influences cochlear turn extension through mechanisms linked to planar cell polarity and neural tube closure.

Conclusion

This research highlights CWC27's critical role in regulating developmental processes, particularly neural tube closure and cochlear development. It underscores the broader importance of spliceosome-associated proteins in shaping normal development and understanding congenital disorders.

S6 L15

Preliminary outcomes of a primary care hearing screening program including 5,360 older adults

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Background: Hearing loss is common and impactful in older adults yet often goes undiagnosed and unaddressed. A pilot hearing screening program was implemented in primary care clinics with an innovative automatic referral to the audiology clinic for further assessment based on patients' responses. This study describes demographic differences in responses to screening questions and preliminary program outcomes.

Materials and Methods: A sequence of 1-4 questions with branching logic was asked of patients ≥65 years of age during visits to primary care clinics at MUSC: 1. Do you think you have hearing loss? If yes, 2. Are you being treated for hearing loss? If no, 3. Would you like a referral to audiology? If no, 4. Why not? If yes, a referral to audiology was automatically generated. We determined demographic differences in responses from patients and from a control group who did not undergo screening.

Results: Of 5,360 patients screened, mean age was 73.0 years, 58.3% female, and 31.2% minority race. Of those screened, 42.3% self-reported hearing loss, and among those, 38.9% reported not being treated for hearing loss. Of those, 53.4% agreed to audiology referrals.

Conclusion: This screening program using simple questions identified a high percentage of patients with perceived hearing loss, many of whom were not treated. Over half requested audiology referrals when prompted. Additional results will include demographic differences in response to screening questions, other outcomes of this program, including the reasons for denying a referral, and impacts of screening on seeking further audiology assessment and treatment uptake.

S6 L16

Screening for NOX3 inhibitors for the prevention of acquired sensorineural hearing loss

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Background. NAPDH oxidases (NOX), a family of enzymes which sole function is to produce reactive oxygen species (ROS), emerged as a relevant therapeutic target to treat or prevent acquired forms of sensorineural hearing loss, such as age-related or noise-induced, among others. The NOX3 isoform is only expressed in the inner ear, making it a promising target for pharmacological inhibition for otoprotection, notably by preventing ROS-induced damage to the auditory synapse. This project aims at discovering NOX3 small molecule inhibitors.

Methods. We developed a cell-based high-throughput screen relying on the detection of extracellular superoxide radical anion ($O_2^{\bullet-}$) generated by NOX3 activity, using the colorimetric assay WST-1. Hits were further tested in dose-response using WST-1 and validated in orthogonal assays detecting hydrogen peroxide (Amplex Red/HRP and CBA fluorometric assays), antioxidant activity and cytotoxicity to eliminate off-target compounds. The selectivity of the validated hits for NOX3 over the 6 other isoforms was also assessed.

Results. Among the 20'511 compounds screened, 125 showed an inhibitory activity on NOX3 equal to or higher than 50% and were considered as hits. One selective NOX3 inhibitor with a micromolar range potency was identified in cell-based assays. Its characterization in ADME studies revealed a good permeability but a poor solubility and metabolic stability in vitro. These aspects are being improved by medicinal chemistry before testing in an animal model of acquired hearing loss.

Conclusion. This screening campaign for NOX3-inhibitors opens new avenues for the development of small molecule therapeutics for the prevention of acquired sensorineural hearing loss.

S6 L17

Precise genetic control of ATOH1 enhances maturation of regenerated hair cells in the mature mouse utricle

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Background: Dizziness and vestibular hypofunction are prevalent inner ear disorders. Vestibular hair cells are mechanoreceptors critical for detecting head position and motion. In the mammalian vestibular organ utricle, hair cell loss causes vestibular dysfunction as spontaneous regeneration is nearly absent. To stimulate regeneration, we and others have shown that constitutive expression of exogenous ATOH1, a hair cell transcription factor, increases hair cell regeneration, however, regenerated hair cells fail to fully mature.

Materials and Methods: Here, we first profiled the mouse utricle at 14 time points, and defined transcriptomes of developing and mature vestibular hair cells. To mimic native hair cells which downregulate endogenous ATOH1 as they mature, we engineered viral vectors carrying the supporting cell promoters GFAP and RLBP1 that allow transient ATOH1 expression and compared them to the ubiquitous promoter CMV. Using adult mouse utricle explants and an in vivo damage model, we examined the effects of these viral vectors on hair cell regeneration and maturation.

Results: In utricles damaged ex vivo with gentamicin, both CMV-ATOH1 and GFAP-ATOH1 increased regeneration more effectively than RLBP1-ATOH1, while GFAP-ATOH1 and RLBP1-ATOH1 induced hair cells with more mature transcriptomes. In utricles damaged in vivo, GFAP-ATOH1 induced regeneration of hair cells expressing genes indicative of maturing type II hair cells, and more hair cells with bundles and synapses than untreated organs.

Conclusion: Together our results demonstrate the efficacy of spatiotemporal control of ATOH1 overexpression in inner ear hair cell regeneration

S6 L18

Superoxide Dismutase AAV gene therapy prevents cumulative hearing loss during repeated noise exposures.
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BACKGROUND: One leading cause of hearing loss in younger adults occurs through recreational and occupational noise exposure that leads to cumulative superoxide damage in the inner and outer cochlear hair cells. Superoxide dismutase (SOD) catalyzes harmful superoxides into nonharmful oxygen and hydrogen peroxide. Thus, we have developed a hair-cell targeted AAV to express the transgene for SOD enzymes. In this study, we have treated adults that are already affected by hearing loss to determine if SOD gene therapy offers neuroprotection from further exposures to damaging levels of noise.

MATERIALS & METHODS: Adult (P86) Mongolian gerbils (Meriones Unguiculatus) received baseline auditory brainstem response recordings followed by five days of noise exposure (110 dB SPL, 2 hours). After four weeks of recovery the gerbils underwent cisterna magna injections of either saline or AAV-based SOD1 (intracellular), SOD2 (mitochondrial), or SOD3 (extracellular) gene therapy. After three weeks of transgene expression, animals were then again given five days of noise exposure (110 dB, 2 hours). Recordings were carried out at one- and four-weeks post exposure for both rounds to quantify transient and permanent threshold shifts.

RESULTS: Compared to controls, SOD transgene expression offered significant protection from initial hearing loss (prophylactic) and from further hearing loss (treatment) in animals that already had mild to moderate increases in auditory thresholds.

CONCLUSION: These data suggest that individuals that are at risk for occupational or recreational noise-induced hearing loss, or already have mild to moderate hearing loss, will benefit from this inner ear gene therapy.

S6 L19

From Hearing to Memory: Examining the Cognitive Impact of Presbycusis in the Polish PURE Cohort

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Background:

Age-related hearing loss (ARHL) is one of the most prevalent chronic conditions in older adults. It has recently been identified as a potentially modifiable risk factor for cognitive impairment and dementia. This study aimed to investigate the association between ARHL and cognitive performance in the Polish arm of the PURE (Prospective Urban and Rural Epidemiological) study.

Methods:

The analysis included 891 participants from the PURE Poland cohort, aged 40–79, residing in Wrocław and nearby rural areas. Hearing loss was assessed through self-report and the use of hearing aids. Cognitive function was evaluated using a comprehensive battery, including the Montreal Cognitive Assessment (MoCA), Digit Symbol Substitution Test (DSST), Trail Making Test (TMT), the Centre for Epidemiological Studies Depression Scale (CES-D), and the Self-administered Gerocognitive Exam (SAGE). Participants were also evaluated for cardiovascular and metabolic comorbidities.

Results:

Hearing loss was significantly associated with lower cognitive scores across all tested domains. Individuals with ARHL had a 1.34 times higher odds of mild cognitive impairment (MoCA <26). Their mean MoCA score was 0.52 points lower than those without hearing loss. ARHL was more common in men and those with hypertension, diabetes, or obesity. Additionally, ARHL was linked to increased depressive symptoms and reduced functional independence.

Conclusions:

ARHL is independently associated with cognitive decline and should be considered a key target for dementia prevention. Routine hearing screening after midlife, alongside interventions addressing vascular and metabolic health, may help mitigate cognitive deterioration and improve overall quality of life in aging populations.

S6 L20

Cochleovestibular dysfunction in patients with primary mitochondrial disease due to pathogenic mitochondrial DNA variants.

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Background: Primary mitochondrial diseases (PMD) are a heterogenous group of disorders affecting the mitochondria through pathogenic variants either in nuclear DNA (nDNA) or in mitochondrial DNA (mtDNA).

Material and Methods: We have investigated the effects of PMD on hearing and balance in one retrospective and one prospective cohort.

Results: In PMD patients seen at The Children's Hospital of Philadelphia, USA, we demonstrated that in PMD due to pathogenic variants in mtDNA, onset of hearing loss was invariably post-lingual. This has important implications for the investigation of children and young adults with sensorineural hearing loss (SNHL), as genetic cause (mtDNA) has to be considered despite the child passing the newborn screen, and that whole genome sequencing also covering mtDNA should be considered the gold standard for investigation.

That hearing loss is a common feature of PMD is relatively well-described. In our retrospective cohort, SNHL was audiometrically confirmed in 20% of patients with pathogenic mtDNA variants, and in 58% of mtDNA deletions. Less is known about the vestibular function in patients with PMD. In an ongoing prospective cohort of patients with PMD due to pathogenic mtDNA variants (primarily m.A3243A>G) at Skåne University Hospital, Sweden, to date 100% of subjects lack response to cVEMP on at least one side, while only 17 % had pathological vHIT.

Conclusion: SNHL is common in PMD, and vestibular dysfunction may be an underreported phenomena in this patient group. Gait disorders in PMD is normally attributed to myopathy and fatigue, but vestibular dysfunction is likely contributing.

S6 L21 WITHDRAWN

Nasal obstruction and anxiety – Is there a link?

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Introduction: Most patients complaining of nasal obstruction have anatomical factors such as polyps or a deviated septum, explaining the symptoms. In contrast, certain patients without any evident anatomical factor complain of nasal obstruction. It is hypothesized that a dysfunctional respiratory pattern (hyperventilation) may explain part of their perceived nasal obstruction.

Methods: We examined three groups of patients complaining of nasal obstruction, the first on with nasale polyps (n=34), the second with obvious septal deviation (n=34) and the third without any major anatomical abnormality (n=34). We measured airflow and trigeminal function and questionnaires for nasal symptoms (NOSE) and breathing related anxiety (Nijmegen).

Results: The third group, complaining of nasal obstruction without any major anatomical explanation for the symptoms had similar respiratory and trigeminal and NOSE outcomes but significantly higher anxiety scores.

Conclusion: The present data suggest, that in a subgroup of patients with nasal obstruction, anxiety may play a role for the breathing complaint. This seems especially to be the case if no major anatomical or inflammatory factor explains the nasal obstruction.

S7 L1

Transoral Robotic Surgery and Neck Dissection for Hypopharyngeal Cancer: Long-Term Prognostic Factors and Survival Outcomes.

Chen-Chi Wang

Background: Transoral robotic surgery (TORS) with neck dissection has emerged as an organ-preserving treatment for hypopharyngeal cancer since a decade ago. This study analyzes long-term prognostic factors to improve management.

Material and Methods: From October 2010 to August 2023, 48 patients with T1-T3 hypopharyngeal cancer, without prior upper aerodigestive tract cancer or irradiation, underwent TORS and neck dissection with/without adjuvant chemoradiation. Perioperative parameters, pathology, adjuvant therapy rates, and survival outcomes were retrospectively analyzed.

Results: Among 48 patients, 37.5% had T1, 45.8% had T2, and 16.7% had T3 tumors. Complete tumor resection was achieved in all cases. Pathologic staging showed 50% had early-stage (I/II) and 50% had late-stage (III/IV) disease. Radiotherapy was spared in 47.92% of cases. After a mean follow-up of 5.9 ± 3.5 years, 5-year overall survival and disease-specific survival rates were both 77%, with a recurrence-free survival rate of 69%. Recurrence was significantly associated with pathologic stage, N stage, and extra-nodal extension ($p<0.05$). Fifteen patients died, with only two (13.3%) due to local recurrence, one (6.7%) from unrelated causes (Flu), seven (46.7%) from distant metastases, and five (33.3%) from secondary primary cancers.

Conclusion: TORS with neck dissection had low primary recurrence, achieving a 5-year overall survival of 77%. Distant metastases and secondary malignancies remain major causes of mortality.

Keywords: hypopharyngeal cancer; organ preservation; survival rate; transoral robotic surgery; extra-nodal extension

S7 L2

Surgical Salvage for HPV-associated Oropharyngeal Cancer: What is the Evidence

C. René Leemans, Simone Eerenstein

Background: Radiotherapy or chemoradiation is the current treatment of choice for oropharyngeal squamous cell carcinoma (OPSCC). Salvage surgery for residual or recurrent disease is possible in a minority of patients only, technically challenging and associated with high complications and poor prognosis. The aim of our study was to evaluate the efficacy of salvage surgery and determine survival outcomes for patients with residual or recurrent oropharyngeal squamous cell carcinoma (OPSCC) after primary (chemo)radiotherapy, since the shift from surgical to non-surgical treatment from the early 2000s.

Patients and Methods: This is a single institution retrospective study of patients treated in Amsterdam UMC with residual or recurrent OPSCC after (chemo)radiation who had salvage surgery. We reviewed the data of patients between 2000-2023. Short and long-term complications were recorded. Kaplan-Meier analysis was used to determine overall survival and recurrence-free survival. Univariate analysis was performed using Cox proportional hazard regression.

Results: Sixty one patients underwent salvage surgery: twenty four underwent local resection and neck dissection, thirty six with regional tumor underwent neck dissection and one patient had local resection only. Post-operative complications occurred in 31 patients (50.8%): fistula formation in 4 patients 6.6% and flap-failure in 5 patients (8.2%). Five-year overall survival for all patients was 38.9%. PEG-tube and tracheotomy-dependency persisted after salvage in 43.3% and 12%. 5-year survival in R0-, R0 with clear margins and in R1-resections was 43.0%, 19.0% and 28.6% respectively. 5-year survival for N-stage at time of salvage surgery for equal, lower and higher vs primary N-stage was 58.8%, 30.3% and 19.4% ($p = 0.011$). 5-year survival for HPV+ tumors and for HPV- tumors was respectively 53% and 33.5% ($p = 0.074$).

Conclusion: Although salvage surgery is highly complex, may come at the toll of remaining PEG-tube or tracheotomy dependent, it does offer the patient the best opportunities for survival in cases of residual or recurrent OPSCC. In our institution almost 40% of all salvage-patients achieved 5-year survival.

S7 L3

Adjuvant Everolimus in Advanced-Stage Head and Neck Squamous Cell Carcinoma: Clinical and Preclinical Evaluation of Efficacy and Immune Modulation

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Background: Advanced-stage p16-negative head and neck squamous cell carcinoma (HNSCC) patients face high recurrence risk following definitive therapy. There are no established adjuvant strategies to mitigate this risk after complete response to initial therapy. As the Akt/mTOR pathway is frequently dysregulated in HNSCC, we aimed to evaluate whether adjuvant everolimus improves progression-free survival (PFS) and elucidate its immunomodulatory effects.

Materials and Methods: A prospective, randomized double-blind phase II trial enrolled 52 patients with advanced HNSCC from 2010 - 2015. Patients, confirmed disease-free post-definitive therapy, were randomized to oral everolimus (10 mg/day) or placebo for up to one year. p16 immunohistochemistry and whole-exome sequencing were performed. The primary endpoint was PFS, with secondary endpoints including overall survival and toxicity. Preclinical studies utilizing PD-1-resistant ROC-1 syngeneic tumor grafts were conducted to assess the immunological impact of everolimus.

Results: Everolimus demonstrated a trend toward improved PFS (HR = 0.44; P = 0.093), with statistically significant benefits in p16-negative (HR = 0.26; P = 0.031) and TP53-mutated (HR = 0.24; P = 0.027) patients. Preclinical investigations demonstrated that everolimus inhibited anti-PD-1 resistant ROC-1 tumor growth, increased CD8+ T cell infiltration, upregulated class-I MHC expression, and reduced PD-1+ exhausted T cells. Moreover, tumor-infiltrating lymphocytes from everolimus-treated mice exhibited significantly enhanced cytotoxicity in co-culture assays.

Conclusion: Everolimus may confer clinical benefit in high risk p16-negative HNSCC patient subsets while modulating antitumor immunity. These findings provide strong rationale for further investigation of mTOR inhibition as an adjuvant therapeutic strategy in HNSCC.

S7 L4

Mesenchymal Stem Cells for the Treatment of Xerostomia

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Background

Xerostomia causes debilitating symptoms and reduced quality of life (QoL). The most common causes are radiotherapy for head and neck cancer and Sjögren's disease (SjD). Up to 80% of head and neck cancer patients develop xerostomia post-radiotherapy, and approximately 0.5% of the Western population suffers from SjD. Current treatments are limited, prompting investigation of intraglandular mesenchymal stem cell (MSC) therapy in both groups.

Methods

Three randomized controlled trials (RCTs) were conducted in patients with radiation-induced xerostomia. Participants were randomized 1:1 to receive ultrasound-guided injections of allogeneic MSCs or placebo into the submandibular glands. The primary outcome was unstimulated whole salivary flow rate (UWS); secondary outcomes included stimulated saliva and patient-reported QoL. A separate RCT targeting SjD-related xerostomia is ongoing.

Results

In total, 160 patients with prior head and neck cancer were included. MSC-treated patients showed a significant increase in UWS, whereas placebo-treated patients did not. Both groups reported symptom improvement, but no statistically significant differences were found between MSC and placebo groups. No serious adverse events related to treatment occurred.

Conclusion

Intraglandular MSC therapy is safe and led to significant improvements in salivary flow and symptoms. However, superiority over placebo could not be confirmed. A Phase II trial is underway evaluating two MSC treatments, and a Phase 1/2 trial in patients with SjD is ongoing. Larger, multicenter trials are needed to confirm these findings.

S7 L5

The usefulness of Novel Continuous and Quantitative Intraoperative Facial Nerve-Monitoring System for facial nerve schwannoma surgery

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The intra-temporal facial nerve schwannoma could result in several symptoms causing deterioration of the QOL of the patient, such as facial nerve palsy or conductive hearing loss. Usually, a small tumor can be managed by the “wait and scan” policy. The surgical intervention would be applied for growing or relatively large tumors or symptomatic cases.

Total resection must cause severe facial nerve palsy and will be applied in limited cases. In contrast, subtotal resection would sometimes be used as a surgical intervention. However, subtotal resection also would cause facial nerve palsy as a surgical complication. Therefore, decision-making on “when” and “how” to treat with surgery would be difficult.

So far, we reported the usefulness of continuous and quantitative intraoperative monitoring for the tumor resection of the temporal bone lesions (Hosoya M et al., European Archives of Oto-Rhino-Laryngology, 2025). In this study, we applied this system for facial nerve schwannoma surgery.

Materials and Methods

We retrospectively analyzed the cases of facial nerve schwannoma with surgical interventions in our department using this novel monitoring system. Case details, electrode placement sites, and facial nerve function data were obtained and retrospectively evaluated before and after the surgery.

Results

By using this continuous monitoring system, post-operative facial nerve functions can be preserved in most cases.

Conclusion:

The advantages of this system include its ability to perform quantitative intraoperative evaluations and prevent unexpected nerve damage in cases where the facial nerve shows complicated pathways. This monitoring system is useful in intra-temporal facial nerve schwannoma.

S8 L1

Image guided surgery in oral cancer
Remco de Bree

Resection margins of oral squamous cell carcinoma (OSCC) are often inadequate. Especially, obtaining free deep resection margins is challenging. In a conventional setting, the deep margin can be estimated intraoperatively by usage of preoperative imaging, visual inspection, and palpation. Frozen section analysis (FSA), utilized by many surgeons, allows intraoperative analysis of resection margins for residual tumor tissue, but has limited additional value. The ideal intraoperative imaging technique for OSCC is able to guide the resection real time and is applicable for intra-operative ex-vivo for margin assessment. Both ultrasound and fluorescence are able to image the tumor intraorally and perform ex-vivo imaging of the resection specimen. Fluorescence is also able to image residual tumor tissue in the wound bed. MRI can only be used on the ex-vivo specimen.

Several small studies on fluorescence imaging for intraoperative margin assessment in OSCC patients were performed. A feasibility study and pilot study showed that ultrasound-guided resections of tongue cancer may improve margin status and reduce the need for re-resections and adjuvant radiotherapy. A Dutch multicenter randomized clinical trial comparing conventional resection and ultrasound guided resections of tongue cancer finished accrual. Preliminary results will be presented. A multicenter study of ultrasound guided resections of buccal cancer is ongoing. A monocenter study on the ex-vivo use of MRI for margin assessment was recently started. Some cases will be presented.

S8 L2

Machine learning for predicting overall survival in early-stage supraglottic laryngeal cancer: A SEER-based population study

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Background: Supraglottic squamous cell carcinoma (SGSCC) represents the second most prevalent form of laryngeal cancer. Early-stage SGSCC is prone to local spread, cervical lymph node metastasis, and resistance to chemotherapy, which all contribute to poor prognosis. Prediction of overall survival (OS) in early-stage SGSCC may facilitate targeted treatment. This study aimed to combine clinicopathological and treatment-related factors as integrative inputs to build a machine learning (ML) model to estimate the OS of patients with SGSCC. Furthermore, we explored the complementary prognostic potential of these input parameters for OS. Materials and Methods: A total of 1171 patients with SGSCC were extracted from Surveillance, Epidemiology, and End Results (SEER) public data to predict OS. We used feature importance analysis to examine the integrative inputs that are associated with OS. Results: The ML showed a weighted accuracy of 82.2% in predicting OS. The aggregate feature importance showed that age at diagnosis, marital status, tumor count, surgical treatment, and radiation are the five most important features for enhancing OS among these patients. We found that as the age increases, the chance of OS decreases. Being married, fewer tumor count, surgical treatment, and radiotherapy were all associated with improved OS. Conclusion: Combining clinicopathological and treatment-related factors seems to accurately predict OS in patients with early-stage SGSCC. Having prior information on the OS of these patients could help in tailoring personalized treatment strategies and potentially improving treatment outcomes. Despite the accuracy of our ML model, external independent geographic validation is warranted to evaluate its generalizability.

S8 L3

Nordic Oropharyngeal Squamous Cell Carcinoma Cohort

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Introduction:

For the past decades, the incidence of oropharyngeal squamous cell carcinoma (OPSCC) has been increasing worldwide, especially in the Nordic countries. Despite much research, many questions have not been answered and validated in larger, multicenter cohorts using both p16- and HPV-status.

Multiple separate cohorts exist in the Nordic countries. Further, a public health system across the Nordic countries secures equal access, and national health registries with automatic reporting ensures high follow-up rate and high quality of data. Hence, there is a large potential in creating a comprehensive Nordic OPSCC cohort.

Materials and methods:

In this method study we compile multiple OPSCC cohorts in Denmark, Sweden, Finland, Norway, and Iceland creating a large multinational cohort. An extensive list of variables are being collected and we strive to ensure HPV and p16 status on all patients. Patients from 2000 to 2023 are included.

Results:

8400 patients are included in the cohort. It is estimated that >9000 patients will be included in total. Further, 8 studies are scheduled, and more are being planned. Studies are planned to commence in September.

Conclusion:

Many research questions in HPV induced OPSCC warrants further research. As a result of the common Nordic public health system and automatic reporting to national databases, there is a large potential for compiling cohorts with a high follow-up rate, thereby enabling high-quality multicenter research in much warranted questions. Hence, the results of this Nordic OPSCC collaboration will have the potential to guide future treatment protocols.

S8 L4

Prognostic value of T regulatory cells and immune checkpoints expression in tumor-draining lymph nodes for oral squamous cell carcinoma

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Despite the employment of extensive therapeutic strategies, OSCC recurrence and mortality rates persist at high levels. This underscores the shortcomings of current prognostic models and the urgency for refined biomarkers. This study explores the prognostic significance of tumor-draining lymph nodes (TDLNs) in OSCC, with a special focus on the quantification of T regulatory cells (Tregs) and the expression of immune checkpoints on T cells.

Methods: Forty-nine OSCC patients were enrolled. One TDLN per patient was analysed using flow cytometry to profile immune-checkpoint expression (PD-1, CTLA-4, TIGIT, TIM-3, LAG-3) and other markers such as CD69, CXCR5 on CD4+, CD8+, and Tregs. Disease-free survival (DFS) and overall survival (OS) were assessed.

Results: According to multivariate analysis, elevated levels of FoxP3+CD4+ and TIGIT+CD8+ cells in TDLNs correlated with significantly worse DFS, while high CXCR5+CD4+ levels were associated with better DFS. Notably, the expression of immune checkpoints on T cells within TDLNs showed significant associations with recurrence status. Patients experiencing recurrence exhibited heightened levels of T regulatory cells, CD4+PD -1+ and CD4+CTLA-4+, cells in TDLNs. Survival multivariate analyses revealed that T status emerged as an independent predictor of OS.

Conclusion: The findings highlight the critical role of TDLNs in the immune microenvironment of OSCC and establish immune checkpoint expression on T cells as promising prognostic biomarkers. These insights upgrade the prognostic framework for OSCC and pave the way for individualized therapeutic strategies. The prognostic significance of TDLNs and a high expression of immune checkpoint inhibitors is a compelling argument for the adoption of neoadjuvant immunotherapy.

S8 L5

Temporal muscle thickness as a Prognostic Factor in Patients with Head and Neck Squamous Cell Carcinoma Treated with Immune Checkpoint Inhibitors

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Background:

Malnutrition, particularly reduced muscle mass, is a common issue among patients with recurrent or metastatic head and neck squamous cell carcinoma (R/M HNSCC), often exacerbated by previous treatments. Temporal muscle thickness (TMT) has recently emerged as a surrogate marker for skeletal muscle mass and may hold prognostic value. This study aimed to investigate the prognostic significance of TMT in patients with R/M HNSCC treated with immune checkpoint inhibitors (ICIs).

Methods:

A retrospective analysis was conducted on 109 patients with R/M HNSCC who received nivolumab or pembrolizumab between 2017 and 2023. TMT was measured on axial CT scans at the Sylvian fissure level. Patients were grouped into high and low TMT categories based on sex-specific cutoff values derived from ROC analysis. Associations between TMT and clinical outcomes—including objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and overall survival (OS)—were analyzed.

Results:

High TMT was significantly associated with a better response to ICI therapy. Patients with high TMT demonstrated improved 1-year PFS (36.5% vs. 15.8%, p = 0.010) and OS (73.1% vs. 47.4%, p = 0.001) compared to those with low TMT. Multivariate analysis confirmed TMT as an independent prognostic factor for both PFS and OS.

Conclusions:

TMT is a practical and non-invasive biomarker that can predict clinical outcomes in R/M HNSCC patients undergoing ICI therapy. It may aid in treatment decision-making and patient stratification.

S8 L6

Specificity and sensitivity of circulating HPV-DNA in patients with oropharyngeal squamous cell carcinoma

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Background:

Oropharyngeal squamous cell carcinoma (OPSCC) is one of the most common head and neck cancers and is strongly associated with human papillomavirus (HPV) infection. In Denmark, over 70% of OPSCC cases are now HPV-positive. We have previously shown that cell-free HPV-DNA can be detected in blood at diagnosis, disappears after successful treatment, and reappears months before clinical recurrence. This project aims to implement HPV-DNA testing in the follow-up program to enable earlier detection of recurrence.

Methods:

Newly diagnosed HPV+ OPSCC patients in eastern Denmark (~47% of the national population) are invited to participate. Blood samples are collected at baseline and at 2, 6, 12, 18, 24, 30, and 36 months post-treatment—or earlier if recurrence is suspected. Samples are analyzed using a validated ddPCR assay targeting HPV types 16, 18, 31, 33, 35, 45, 51, and 58. Positive samples trigger further clinical evaluation with ENT examination and PET/CT scan. Quality of life is assessed using the Fear of Recurrence Questionnaire.

Results:

To date, 140 of the planned 200 patients have been enrolled, with an ~80% participation rate. Most refusals occur due to patients feeling overwhelmed at diagnosis. All head and neck centers in eastern Denmark are now collaborating on blood collection. The assay has been fully implemented in the lab. No recurrences have been detected thus far. Sensitivity is consistent with prior studies from our group.

Conclusion:

Implementation of HPV-DNA testing in clinical follow-up is feasible and well-accepted. Continued follow-up will determine its utility in detecting early recurrences.

S8 L7

Turning the bad tumors good: Systemic treatment to switch HPV+ HNSCC subtype and sensitize resistant tumors to radiation

Wendell Yarbrough, Natalia Issaeva, Travis Schrank, Aditi Kothari, Sri Vemulamanda

- Background

We identified two subtypes of human papillomavirus (HPV+) head and neck squamous cell carcinoma (HNSCC). The subtypes correlate with sensitivity to radiation and survival, and the subtypes many molecular distinctions converge on tumor NF-κB activity. We hypothesize that effecting "subtype switching" from the poor prognosis low-NF-kB subtype to the good prognosis high NF-kB subtype will sensitize tumors to radiation as a novel treatment for HPV+ HNSCC.

- Materials/Methods

Standard models plus our newly developed novel fully immunocompetent mouse model of high-risk HPV+ HNSCC were studied. NF-kB was activated using a Toll-like receptor 5 (TLR5) agonist and second mitochondria-derived activator of caspases (SMAC) mimetics.

- Results

A TLR5 agonist and SMAC mimetics activated NF-κB and sensitized HPV+ HNSCC cells and tumors to radiation prolonging survival in HPV+ HNSCC xenografted mice. Treatment with single agent TLR5 agonist suppressed growth of the poor prognosis subtype of HPV+ HNSCC as effectively as 32Gy of focused radiation.

- Conclusion

Identification of two subtypes of HPV+ HNSCC driven by NF-kB activity offers the opportunity to improve outcome for the poor prognosis group by pharmacologic subtype switching. We found that drugs that activate NF-kB are sufficient to sensitize the poor prognosis subtype to radiation. A TLR5 agonist, entolimod, is FDA approved and was developed to protect normal tissues from radiation. The opposing effects of this TLR on cancer versus normal tissues – radiation sensitization of HPV+ HNSCC and radioprotection of normal tissues – suggest that it may enhance patient survival and decrease radiation-associated side effects.

S8 L9 WITHDRAWN

Intraoperative Margin Detection of Head and Neck Cancer with Dynamic Optical Contrast Imaging: The next Leap Forward for our Patients

Maie St. John

Background:
Oral and Head and neck squamous cell carcinoma (OSCC) is the sixth most common cancer in the world. The primary management of OSCC relies on complete surgical resection of the tumor. However, the establishment of negative margin complete resection is often difficult given the devastating side effects of aggressive surgery and the anatomic proximity to vital structures such as the carotid artery and the spinal cord. Positive margin status is associated with significantly decreased survival. Currently, it is the surgeon's fingers that determine where the tumor cuts are made, by palpating the edges of the tumor. Accuracy varies widely based on the experience of the surgeon and the location and type of tumor. Efficacy is further confounded by the risk of damage to adjacent vital structures, which limit resection margins. The ability to accurately determine whether the excised margins are tumor-free intraoperatively would reduce the risk of recurrence and the need for subsequent surgeries while preserving patient function.

Materials and Methods:
Our group has developed the Dynamic Optical Contrast Imaging (DOCI) technique that can delineate oral cancer margins in clinical fields with a sensitivity and specificity (both > 95%). DOCI is based on quantifiable dynamic temporally dependent tissue autofluorescence measurements that allow the acquisition of specific tissue properties over a large field of view in macroscopic and cluttered, in vivo clinical fields.

Results:
The DOCI system has been studied in an animal model and has been validated in a pilot trial on patients undergoing surgery. Companion visible imagery and histology were analyzed at all stages of the work, ensuring statistical power of DOCI. Obtaining negative surgical cancer margins is the strongest predictor for long-term survival of OSCC patients. Currently, patients can have positive margins after surgery because there is a paucity of specific and intraoperative clinically relevant tools.

Conclusion:
DOCI allows for intraoperative, real-time video rate visualization of malignant and healthy tissue margins to help guide tumor resection. By allowing the surgeon to precisely determine margins intraoperatively, DOCI can directly impact surgical outcomes and improve overall survival for our patients.

S8 L10

Assessing volume growth of paranasal sinuses and nasal cavity in children using three-dimensional imaging software

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Background: Understanding the normal development of the sinuses throughout childhood is necessary to diagnose medical conditions, plan appropriate treatment, and better determine the developmental impact of treatment, including surgery.

Methods: Paranasal sinus and nasal cavity volumes from computed tomography (CT) images in patients aged 0–24 years were measured using a 3D model to examine age-related changes. Paranasal sinus and nasal cavity growth were compared between age groups. Additionally, the correlation between body height and paranasal sinus growth was examined.

Results: A total of 139 CT scans from 137 patients were analyzed. Volume growth of maxillary, ethmoidal, sphenoid, frontal sinuses, and nasal cavity was observed until 18, 16, 20, 20, and 22 years, respectively. Maxillary sinus rapidly grew at 2–8 and 9–12 years, ethmoid sinus 2–8 and 13–16 years, sphenoid sinus 5–8 years, frontal sinus 2–10 years, and nasal cavity 7–12 years. The median volume after growth completion for maxillary, ethmoidal, sphenoid, frontal sinuses, and nasal cavities was 21,937 mm3, 4868 mm3, 5870 mm3, 3172 mm3, and 15,555 mm3, respectively. The left-right difference in the nasal cavity volume increased with age. Sinus and nasal cavity growth completion was delayed by 2–4 years compared to general height growth.

Conclusion: Growth of the ethmoid, maxillary, sphenoid, frontal sinus, and nasal cavity was completed in approximately 20 years. Compared to the results shown in reports based primarily on 2D measurements, the ethmoid and sphenoid sinuses and nasal cavity were found to continue to grow until older age than previously thought.

S8 L11

The role of PTHrP and PTH1R expression in locally advanced laryngeal squamous cell carcinoma: prognostic implications and response to cetuximab therapy

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Introduction:

Parathyroid hormone-related peptide (PTHrP) overexpression has been documented in various human malignancies and is frequently associated with poor clinical outcomes. This study aims to evaluate the expression levels of PTHrP and its receptor, PTH1R, in primary locally advanced laryngeal squamous cell carcinoma (LALSCC), and to assess their correlation with clinical outcomes, particularly in the context of cetuximab-based therapy.

Methods:

A retrospective exploratory analysis was performed on a cohort of 66 patients diagnosed with LALSCC and treated with bio-radiotherapy in combination with cetuximab. Immunohistochemical techniques were employed to examine the expression of PTHrP, PTH1R, and HER1.

Results:

Poorly differentiated tumors—typically associated with unfavorable prognosis—exhibited nuclear localization of PTHrP and lacked PTH1R expression. In contrast, both normal laryngeal epithelium and well-differentiated cancer cells displayed cytoplasmic localization of PTHrP and PTH1R, suggesting a potential autocrine/paracrine function of PTHrP in squamous cell differentiation. Moreover, HER1-positive tumors demonstrated markedly elevated PTHrP expression ($p < 0.0001$), predominantly at the nuclear level, aligning with HER1-mediated upregulation of the PTHrP gene. Multivariate analysis indicated that patients with PTHrP-positive tumors faced a significantly higher risk of disease relapse (HR = 5.49; 95% CI: 1.62–22.24; $p = 0.006$) and reduced overall survival (HR = 8.21; 95% CI: 1.19–105.00; $p = 0.031$).

Conclusions:

Nuclear expression of PTHrP and absence of PTH1R in LALSCC may serve as predictive biomarkers for resistance to cetuximab-containing therapies and may reflect a more aggressive tumor phenotype driven by HER1 signaling pathways.

S8 L12

Functional RNAi Screening Identifies G2/M and Kinetochore Components as Modulators of TNFα/NF-κB Prosurvival Signaling in Head and Neck Squamous Cell Carcinoma

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Background: Immune and radiation resistance of cancer cells to cytotoxicity mediated by TNFα is promoted by the transcription factor NF-κB in head and neck squamous cell carcinoma (HNSCC). Genomic alterations that converge on the TNFα/NF-κB signal axis were found in ~40% of HNSCCs by The Cancer Genome Atlas.

Methods: Here, we conducted a functional RNAi screen to identify regulators of TNFα-induced NF-κB activation and cell cytotoxicity, using parallel NF-κB β–lactamase reporter and cell viability assays in a HNSCC cell line which harbors expression and genomic alterations typically found in human papillomavirus–negative HNSCC.

Results: Besides multiple components of canonical TNFα/NF-κB signaling, we unexpectedly observed that multiple G2/M cell-cycle kinases [Aurora kinase A, polo-like kinase 1, WEE1, and threonine tyrosine kinase (TTK)], and structural kinetochore/microtubule components (NDC80 and NUF2), modulate TNFα-induced NF-κB activation and cell viability. Several of these targets inhibit TNF-induced nuclear translocation of NF-κB RELA, consistent with a link between NF-κB activation, G2/M kinases, and microtubule assembly. WEE1 was found to complex with Inhibitor-κB Kinase-RELA and phosphorylate G2M checkpoint kinase CDC2 in response to TNFα. Further investigation revealed that WEE1 and TTK inhibition or depletion attenuates TNFα-induced RELA nuclear translocation, promoting cell death, DNA damage, polyploidy, and mitotic catastrophe, and radiosensitization.

Conclusions: Together, our study identifies a key linkage between the G2/M/kinetochore components and nuclear NF-κB activition, as well as targets that can sensitize HNSCC cells to TNFα or radiation during this critical cell-cycle checkpoint.

S8 L13

The role of REV7, CD109, and midkine as biomarkers in head and neck cancer

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Background

Few tumor markers beyond HPV status reliably predict head and neck cancer occurrence, treatment response, and prognosis. This study investigates the potential of REV7, CD109, and midkine (MK) as biomarkers.

Materials and Methods

REV7 immunostaining was performed on oropharyngeal cancer specimens to assess correlations with clinical factors. A REV7-knockout human pharyngeal cancer cell line (Fadu) was established to evaluate its effect on proliferation and cisplatin sensitivity. CD109 immunostaining and siRNA knockdown were used to analyze CD109's role in cancer progression. Serum MK levels were measured by ELISA to assess their diagnostic and prognostic value.

Results

High REV7 expression in p16-negative oropharyngeal cancer patients correlated with shorter overall survival ($p=0.03$). REV7 knockout reduced proliferation and increased cisplatin sensitivity, suggesting its role in tumor progression and drug resistance. High CD109 expression was associated with shorter progression-free survival in p16+ oropharyngeal cancer ($p<0.01$), and CD109 knockdown led to decreased cell invasion. Serum MK levels were significantly elevated in head and neck cancer patients, showing better diagnostic performance than SCC antigen and CYFRA21-1, with sensitivity, specificity, and accuracy of 57.3%, 85.3%, and 72.1%, respectively. Furthermore, serum MK value predicted chemosensitivity and recurrence and was identified as an independent prognostic factor.

Conclusion

While further validation is required, our findings suggest that REV7, CD109, and serum MK could serve as promising biomarkers for head and neck cancer, aiding in diagnosis, treatment prediction, and prognosis assessment.

S8 L14

Effectiveness of Neuromuscular Retraining (NMR) in patients with hypoglossal-facial anastomoses

Matteo Alicandri ciufelli

Background: Facial nerve paralysis significantly impacts patients' quality of life. Among the surgical options for facial function restoration, hypoglossal-facial anastomosis is a well-established procedure. However, post-operative rehabilitation is crucial to optimize functional outcomes. This multicenter study analyzes the effectiveness of Neuromuscular Retraining (NMR) in patients undergoing this surgical procedure.

Material and methods: The aim of the research is to assess facial function improvement in patients treated with NMR by comparing scores from standardized evaluation scales, including the House-Brackmann (H-B) and the Sunnybrook Facial Grading System. The study included patients operated on in different hospital centers and followed them for 24 months. The results show that rehabilitation with NMR significantly contributes to improving facial symmetry at rest and voluntary movements, positively impacting the reduction of post-operative synkinesis.

Results: The data indicate that the most significant recovery occurs within the first 12 months, with stabilization of results over time. Additionally, the rehabilitative approach proved fundamental in controlling synkinesis, which often worsens in the long term without specific treatment. Despite some limitations due to variations in rehabilitation protocols across participating centers, the study confirms the crucial role of rehabilitation in managing post-surgical facial paralysis.

Conclusion: Neuromuscular Retraining is an effective treatment for functional recovery after hypoglossal-facial anastomosis, highlighting the need for a standardized rehabilitation protocol to optimize clinical outcomes.

S8 L15

Advanced Surgical and medical treatment of Medullary Thyroid cancer

Medullary thyroid cancer (MTC) exhibits a wide spectrum of biological behavior, ranging from indolent to highly aggressive forms. Surgery remains the cornerstone of treatment for MTC. However, tyrosine kinase inhibitors (TKIs) are increasingly being utilized in advanced cases, both as neoadjuvant and adjuvant therapies. In this presentation, we will share our experience managing advanced MTC, including the role of major surgical interventions and the integration of TKI therapy. We will also review the fundamental principles guiding the use of TKIs in this context.

S9 L1

Local Delivery of Steroids to the Inner Ear via the Medical Device INCAT (Inner Ear Catheter) in Partial Deafness Patients During Cochlear Implantation – Preliminary Results and a Feasibility Study

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Background: The administration of steroids to preserve residual hearing during cochlear implantation has been described, although the results are mixed. Nevertheless, according to current knowledge, steroids may have an important role in reducing post-implantation fibrosis and loss of hearing due to electrode insertion trauma and progressive effects of inflammation.

Aim: The aim of the study was to assess separately the effectiveness and safety of three different algorithms of using steroids and INCAT (a medical device) Medel® in partial deafness patients who underwent cochlear implantation and secondly - the assessment of the impact of the depth of the catheter (INCAT) on hearing preservation after cochlear implantation.

Method: Ten patients underwent a cochlear implantation with an inner ear catheter. Steroid administration followed three different algorithms: 1) methylprednisolone 62.5 mg/ml in solution – 3 patients; 2) methylprednisolone 40 mg/ml in suspension – 4 patients 3) dexamethasone 4mg/ml in solution – 3 patients. Pure tone audiometry (0.125–8 kHz) was performed preoperatively and at the cochlear implant activation (one month after surgery). Hearing preservation was assessed according to the HEARRING group formula. Impedance measurements were taken at two days and one month after surgery.

Results: Patients treated with methylprednisolone 40 mg/ml in suspension showed the best hearing preservation, with 50% achieving complete preservation and 50% partial preservation. This group also had the lowest impedance changes (ranging from 1.06 to 2.11 kΩ). A shorter INCAT insertion depth appeared to be more favorable than a longer one. The smallest changes in the hearing thresholds were observed in the second group (methylprednisolone 40 mg/ml in suspension, Depo-Medrol). Hearing preservation (HP) in all patients at the CI activation was as follows: complete hearing preservation (HP) was observed in 2 patients (20%), partial HP in 5 patients (50%), and minimal HP in 3 patients (30%). No patients experienced total hearing loss at the time of CI activation.

Conclusion: All these considerations suggest that patients treated with methylprednisolone 40 mg/ml in suspension had better outcomes compared to others. The generalizability of the results is limited due to the small sample size and the inability to control for potential confounding variables, e.g. the length of the electrode array. Further studies with larger numbers of subjects are needed to confirm the preliminary results of studies on local administration of steroids to the inner ear.

S9 L2

Molecular imaging-based machine learning predicts cochlear implant outcome in prelingually deaf children

Jae-Jin Song, Ja-Won Koo, Taesup Moon

Background: Numerous factors influence the outcome of cochlear implantation (CI). However, the preoperative functional status of the cerebral cortex has only been investigated in small numbers of subjects. Therefore, the current study aims to reveal functional neuroimaging signatures of speech outcome after CI in prelingually deaf patients using a resting-state (RS) FDG-PET big data-based machine learning and to propose an outcome prediction model.

Materials and Methods: 111 prelingually deaf children underwent pre-CI RS-FDG-PET. This FDG-PET was used to predict 3-year post-CI speech outcome on an open set word and sentence test under auditory-only (A-only) and audiovisual (AV) conditions. Ninety cerebral cortical ROIs were used for analysis. For statistical analysis, a LASSO (Least Absolute Shrinkage and Selection Operator) regression analysis was performed using the average metabolism of the 90 ROIs concerning the 3-year speech outcome.

Results: In prelingually deaf CI users, activations of the superior temporal gyrus, supramarginal gyrus, and inferior frontal gyrus were predictors of higher post-CI 3-year language scores in the A-only condition. In the A-V condition, however, additional activation of the anterior cingulate gyrus was required to show a better speech outcome. Activation of the ventral attention network and the prefrontal top-down modulator is important for better language processing in the A-only condition. In the A-V condition, an additional activation of the salience network is necessary to better understand multimodal information.

Conclusion: FDG-PET-based machine learning can predict CI outcome in prelingually deaf subjects. CI users require additional attention and top-down information processing to better understand impoverished auditory input.

S9 L3

Do Expert Surgeons Perform Better CI surgery? Evidence from an In Vitro Study of 30 International CI Surgeons

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Background

Procedural factors during cochlear implant (CI) electrode insertion can introduce mechanical trauma, potentially compromising residual hearing. This study aimed to characterize the mechanical impact of manual lateral wall electrode insertions to inform evidence-based surgical practice.

Materials and Methods

At an international hearing preservation workshop, 30 experienced CI surgeons performed bilateral implant placement on validated artificial temporal bone models. We measured insertion force, intracochlear pressure, and electrode positioning, and extracted metrics indicative of mechanical stress inducing micro- and macroscopic cochlear trauma. Surgeons rated their own performance, and data on clinical experience were collected.

Results

The cohort had a median of 20 years of CI experience, with 77% having performed over 200 CI implants. Post-insertion steps such as sealing the round window, packing the posterior tympanotomy, and routing the electrode cable, contributed significantly to intracochlear stress. Notably, large intracochlear pressure transients and force variation frequently occurred in the later phases of insertion. No correlation was found between objective metrics and surgeons' subjective performance ratings. However, the least experienced group (<50 implants) performed significantly worse than those with 500–1000 implants.

Conclusion

This first systematic in vitro study of CI array insertion by a large international cohort highlights procedural factors that increase the risk of intracochlear trauma. These insights support the development of evidence-based surgical recommendations to improve hearing and structure preservation and offer benchmark data for future studies.

S9 L4

Intensity-Driven Shifts in Tonotopic Coding in Humans: A Framework for Cochlear Implant Frequency Allocation

Craig Buchman, Amit Walia

Background: Acoustically-evoked electrocochleography (ECochG) can be used to map the tonotopic organization of the cochlea using cochlear implant (CI) electrodes. Animal studies, at limited intracochlear locations, have shown higher stimulus intensities broaden frequency tuning and cause a basal shift in best-frequency (BF) position. This study aimed to demonstrate intensity-dependent BF shifts and spread of excitation in humans, offering a more physiologically relevant approach for CI programming.

Materials and Methods: Nine ears from six subjects with preserved cochlear function were implanted with a perimodiolar, twenty-two electrode array. Following implantation, cochlear microphonic (CM) tuning curves were generated for multiple frequencies and intensities to determine the BF electrode. Intraoperative x-rays localized each electrode using a validated scala tympani model.

Results: At near-threshold (~43 dB SPL), the ECochG-derived tonotopic maps closely matched those predicted by established models (e.g., Greenwood and Stakhovskaya), based on threshold responses. At maximal stimulus, BF locations shifted basally by nearly one octave. Statistically significant differences were observed among maps generated at 43 dB SPL, 58 dB SPL, and 83 dB SPL. Lower frequency stimuli (500 and 1000 Hz) exhibited larger shifts than higher frequencies (2000–4000 Hz). Higher intensities also elicited a broader spatial spread of excitation, whereas near-threshold levels produced more localized responses.

Conclusion: This study confirms/refines animal model studies that show the human cochlear frequency-position function is intensity-dependent for both BF location and the spread of excitation. A fixed frequency-place map used in CI, does not mimic the dynamic, intensity-dependent tonotopic configuration seen in natural cochlear function.

S9 L5

Robotic Electrode Insertion Reduces Trauma in a Cadaveric Cochlear Model

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Background:

To evaluate and compare intracochlear electrode positioning and insertion-related trauma between robotic and manual cochlear implant (CI) electrode insertions using micro-CT imaging and a standardized Electrode Scalar Location (ESL) rating.

Material and Methods:

Twenty fresh-frozen human temporal bones (10 left, 10 right) were implanted with Advanced Bionics Slim J electrodes, using either manual or IotaSoft Plus robotic insertion. Seven left–right pairs were obtained from the same donors; the remaining were matched by cochlear size. Pre-operative cone-beam CT confirmed normal anatomy. Post-insertion micro-CT assessed electrode location using the ESL scale: 0 = scala tympani (ST), 1 = possible trauma, 2 = definite trauma. Paired t-test and Fisher's Exact test was used for statistical comparison.

Results:

Cochlear sizes were similar across groups (mean A-measure 9.32 mm vs. 9.30 mm). Robotic insertions resulted in no ESL 2 cases or tip fold-overs. Manual insertions led to 6/10 ESL 2 cases ($p = 0.020$), indicating scala translocation. Robotic insertions showed more extracochlear contacts (23 across 10/10 insertions) than manual (4 across 4/10; $p = 0.011$) resulting in shallower mean insertion depth angle (mean 324° vs. 430°; $p < 0.01$).

Conclusions:

Robotic-assisted insertions significantly reduced intracochlear trauma and avoided scalar translocations, despite the fragility of cadaveric samples. Increased extracochlear contacts and reduced insertion depth suggest a structure-preserving technique with enhanced control and consistency. Clinical studies are needed to confirm these findings and assess in vivo performance.

S9 L6 WITHDRAWN

LANGUAGE DEVELOPMENT OF CHILDREN WITH COCHLEAR IMPLANT

Takashi Nakagawa

Hearing impaired children with cochlear implant (CI) appear to speak well. However, it is important to evaluate domain of language for precise evaluation.

Objectives

638 hearing impaired children were participated in Research on Sensory and Communicative Disorders (RSCD) project of nationwide. The recruited criteria were followed; (1) age from 48 months to 155 months old, (2) congenital hearing impairment of bilatera hearing level >70 dB. Children unable to complete the test battery were excluded.

Methods

We used a test battery for Japanese language called Assessment Package for LAnguage Development for Japanese chIldreN (ALADJIN). All ALADJIN tests were conducted by trained audiologist. ALADJIN packaged consists on tests for vocabulary, syntax, reading and writing, the Test for Question-Answer Interaction Development (TQAID) and additional disabilities.

Results

285 children (44.7%) used a cochlear implant. Threshold of hearing level with CI was significantly lower than that with hearing aid (HA). Score of word recognition ability was observed when the implanted age was lower than 41 months old. Articulation score of speech was 4.2 times higher among the all children employed in the project. Examination for basic vocabulary (PVT-R) showed significant higher score. However, other domain did not show significant difference between CI and HA groups.

Conclusions

The importance of language education was confirmed. We should pick up the problems in detail and eventually make a problem-oriented intervention programs for each child.

S9 L7

Enhancing Pre-Cochlear Implant Counseling Using the Cochlear Implant Quality of Life (CIQOL) Instrument Suite

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[1] Medical University of South Carolina

Background: Ensuring patients have realistic cochlear implant (CI) expectations is a critical component of the CI evaluation process. The development of the CIQOL instrument suite provides the opportunity to develop an evidence-based approach to pre-CI counseling.

Methods: Prospective cohort study of 60 adult CI users with bilateral hearing loss. Participants completed the CIQOL-Expectations instrument pre-CI and the Decisional Regret (DR) Scale and Satisfaction with Amplification in Daily Living (SADL) at 12 months post-CI. The CIQOL-35 Profile, CNC word and AzBio sentences scores were obtained pre-operatively and 12 months post-CI.

Results: Mean pre-CI CIQOL-Expectations scores exceeded 12-month CIQOL-35 Profile scores for the global, communication, environment, and listening effort domains (d=0.65 to 0.97), with the largest discrepancies in the communication and listening effort domains (Profile scores 15.1 and 16.3 points lower than expected [d=0.93 to 0.97]). Using established cutoff scores, 29% of patients reported a substantial degree of DR 12-months post-CI. Patients without DR had post-CI scores closer to pre-CI expectations across CIQOL domains (d=0.34 to 0.91). Notably, the degree of pre- to post-CI improvement in CNC or AzBio scores did not differ between patients with and without DR. Greater pre-post CIQOL-35 Profile domain improvement was more strongly associated with lower DR than changes in speech recognition scores.

Conclusion: Post-CI functional abilities often fall short of pre-CI expectations. Aligning pre-CI expectations with realistic CI benefits through evidence-based counseling is essential for reducing decisional regret, which can be accomplished using the CIQOL instrument suite.

S9 L8

Cortical Volumetric Changes before and after Cochlear Implantation in Postlingually Deaf Adults

Hong Ju Park

Background: Prolonged auditory deprivation induces neuroplastic changes throughout the auditory system. We aimed to investigate brain morphological changes following peripheral hearing loss. Additionally, recent technological advancements allow patients to undergo MRI after cochlear implantation (CI). We aimed to analyse the volumetric changes in brain MRI after CI, focusing on the speech perception in postlingually deaf adults.

Materials and Methods: We conducted a retrospective analysis of magnetic resonance imaging (MRI) data from 47 adults with over 10 years of acquired bilateral severe to profound sensorineural hearing loss (bilateral deaf, BD) and 73 normal hearing (NH) controls. We also enrolled 16 patients who underwent unilateral CI to analyze speech perception ability-related volumetric changes of the brain cortices after CI.

Results: We observed thinner CT in the bilateral superior temporal gyri and lateral occipital cortices, along with significant reductions in CV in the bilateral superior temporal gyri, superior parietal cortices, and lateral occipital cortices in BD patients compared to NH controls. Additionally, subcortical volumes of the thalamus, hippocampus, and amygdala were significantly reduced in BD patients. When analyzing the contralateral cerebral hemisphere before and after CI, a substantial increase in superior frontal gyrus and STG volumes was observed in the left CI group.

Conclusions: Our findings reveal significant structural changes in the brains of BD individuals, affecting key areas involved in auditory processing and the integration of somatosensory and visual information. We also demonstrated that improvement in auditory performance after CI is accompanied by structural restoration in the central auditory structures.

S9 L9

Drug Y Eluting Electrode Provides Otoprotection in a Preclinical Rat Model of Cochlear Implantation

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Background: Cochlear implant (CI) electrode insertion can cause mechanical trauma, triggering oxidative stress and apoptosis that contribute to residual hearing loss. Drug-eluting electrodes offer a promising strategy for otoprotection. This study investigates the efficacy of Drug Y, incorporated into a drug-eluting electrode, in preserving hearing and reducing cochlear damage in a rat model of electrode insertion trauma (EIT).

Materials and Methods: Rats were divided into groups: a control group implanted with a standard electrode and a treatment group implanted with a Drug Y-eluting electrode. Auditory brainstem response (ABR) thresholds were recorded preoperatively and up to 4 weeks post-implantation at different frequencies. Cochleae were harvested for whole-mount immunostaining to quantify sensory cell counts and subjected to immunohistochemical analysis of oxidative stress (8-isoprostane) and apoptosis (cleaved caspase-3).

Results: Rats implanted with the Drug Y-eluting electrode demonstrated significantly lower ABR threshold shifts across tested frequencies compared to controls. The number of outer and inner hair cells were significantly higher in animals receiving Drug Y eluting compared to rats implanted with a standard electrode. Histological evaluation revealed decreased 8-isoprostane and cleaved caspase-3 staining in the treatment group, indicating reduced oxidative stress and apoptosis.

Conclusion: Drug Y delivered via a drug-eluting CI electrode effectively reduces cochlear trauma associated with EIT in a rat model, preserving hearing thresholds and attenuating sensory cell loss. These findings support the potential utility of Drug Y in enhancing hearing preservation during CI. Future studies will focus on pharmacokinetics of Drug Y within the cochlear environment, optimal dosing, and safety profile.

S9 L10

Robotic-Assisted Insertion of Cochlear Implant CI632: an ex-vivo study

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Background:

The precision and stability offered by robotic systems in cochlear implant surgery have the potential to significantly enhance surgical outcomes by minimizing trauma to intracochlear structures. This study presents the first robotic-assisted insertion of the CI632 array (Cochlear) using the RobOtol system (Collin medical), equipped with a novel insertion tool designed to optimize electrode array placement.

Methods:

Ten insertions were performed on temporal bones using the RobOtol system. A micro-Ct was performed after array insertion. The cochlear dimensions (A values) and insertion angles were recorded.

Results:

The new tool, integrated with RobOtol, could yield to controlled and precise insertion movements. It facilitated array insertion and sheath retraction by semi-automating a procedure that typically requires two-handed coordination. Postoperative Micro-CT imaging indicates successful insertions in all cases with the robotic system across varying cochlear dimensions. The mean A distance was 9.1 +/- 0.2 mm. The mean insertion angle was 359 +/- 85 °. The mean first electrode round window distance was 1.4 +/- 1.1 mm. No vestibular translocation was observed. No tip-foldover was observed.

Conclusion:

This study marks the first successful robotic-assisted insertion of the CI632 cochlear implant using the RobOtol system with a new insertion tool. The findings suggest that robotic assistance can enhance the precision and safety of precurved array designs, offering a promising avenue for future clinical applications. Further research is warranted to validate these results in clinical settings and to explore the long-term benefits for patients.

S9 L11

Modulation of immune/inflammatory responses to cochlear implantation in animals and humans.

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Background: Placement of an electrode array (EA) in the cochlea leads to a chronic immune/inflammatory response that can limit the function of the device and cause loss of residual cochlear function. This response can be characterized as an 'ectopic lymphoid structure' involving neovascularization, neolymphangiogenesis, and infiltration of a myriad of activated immune cells including macrophages, lymphocytes, and dendritic cells. We have investigated various methods to mitigate this response.

Materials and Methods: Electrophysiology and histology of cochleae following cochlear implant with dexamethasone eluting (Dex-EA) or thin film coated EA.

Results: Dex-EA leads to sustained reduction in impedance in humans and mice and nearly completely suppresses cochlear inflammation and fibrosis in mice. These effects are sustained for at least 6 months in mice and 12 months in humans. Meanwhile, treatment with the CSF1R inhibitor, PLX5622, effectively depletes macrophages in mouse cochleae yet fails to prevent fibrosis and increased electrode impedances. Finally, we have developed a photodriven method to covalently graft zwitterionic thin film coatings to EA. The coating is durable and mitigates biofouling by reducing protein and cellular adhesion, targeting the initial steps underlying the chronic inflammatory response to biomaterials. In mice and sheep, the thin film coating significantly reduces inflammation and fibrosis. It also reduces electrode impedances by ~50%.

Conclusions: Together these data suggest that broad targeting of the inflammatory response with Dex-EA or alteration of the surface properties of EAs with a thin film coating each effectively reduce intracochlear inflammatory responses associated with implantation of EA biomaterials.

S10 L1

Functional Outcome in a Rationally Designed Genomically Humanized Mouse Model for Dominantly Inherited Hearing Loss DFNA9.

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Background: DFNA9 is the most frequent hereditary autosomal dominant hearing disorder in Belgium and the Netherlands causing hearing loss at 20-30 years and evolving towards severe-to-profound sensorineural hearing loss by 60-70 years. Additionally, patients suffer from bilateral vestibulopathy by the age of 40 years. In the Dutch/Belgian population, the c.151C>T

founder mutation in the COCH gene is the most prevalent variant.

Methods: A partial (4 exons) genetic humanisation of the COCH gene was generated in C57Bl6 background (corrected for Cdh23), including wt mice, as well as heterozygous and homozygous c.151C>T variants.

Results: At 9 months, all humanized Coch genotypes showed hearing thresholds comparable to wild-type C57BL/6 Cdh23753A>G mice. This indicates that both the introduction of human wildtype COCH, and correction of Cdh23ahl in the humanized Coch lines was successful. Follow-up on ABR and DPOAE up to 24 months will be presented.

Conclusions: Overall, our approach proved beneficial in eliminating potential adverse events of genomic humanization of mouse genes, and provides us with a model in which sequence-specific therapies directed against the human mutant COCH allele can be investigated irrespective of the phenotype.

S10 L2

Rare and low-frequency genetic variants in families with otitis media

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Background: Otitis media (OM) is a frequent diagnosis in children that causes significant morbidity but remains understudied as a genetic trait despite significant heritability in families. Our aim was to identify rare or low-frequency genetic variants that confer susceptibility to OM.

Methods: Exome sequence data of 287 individuals from 243 families were analyzed. Identified variants were tested for co-segregation with OM in family members. Genome sequence data from a case-control cohort was imputed and analyzed for association of specific genes with OM. Single-cell RNA-sequence data of identified genes were noted in acutely infected mouse middle ears.

Results: Thirty-three variants within 24 genes co-segregated with OM in 28 families, of which 18 variants were considered pathogenic or likely pathogenic. Eighty-one variants in 21 of the same genes were identified in 83 unrelated probands with OM. Of the 24 genes, twelve were associated with OM in mouse models, while fifteen genes were replicated from previous human studies. A common variant EYA4 c.829G>A was associated with OM in the case-control cohort. Using network analysis, twenty-two of the 24 genes were connected in a subnetwork enriched in various signaling pathways, Th1/Th2/Th17 cell differentiation and viral infections. Majority (87.5%) of the identified genes were expressed in mouse middle ear cells, with differential expression after acute infection.

Conclusion: The identification of novel genes and variants for susceptibility to OM will be useful in risk screening and clinical management in children that require a personalized approach due to poor response to standard treatments.

S10 L3

REGULATION OF MUCIN GENES BY CHROMATIN ACCESSIBILTY DURING OTITIS MEDIA

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Introduction. Mucus secreted by middle ear (ME) epithelial cells forms a first line of infection defense. Transmembrane mucins shield the mucosa, while secreted mucins trap and export pathogens via the Eustachian tube. Mucins produced by each of the several ME mucosal epithelial cell types, and how they are regulated during otitis media (OM), are not well understood.

Methods. We assessed single-cell mRNA expression throughout an episode of acute OM induced in mice by nontypeable Haemophilus influenzae (NTHi). We also assayed transposon-accessible chromatin (ATAC) in exposed DNA in normal ME and 24 hours after NTHi infection. We compared altered mucin gene expression with changes in genomic DNA accessibility and transcription factor (TF) gene expression.

Results. Transcriptomes classified ME epithelial cells as high-secretory, low-secretory, intermediate, ciliated or basal. Expression of transmembrane Muc1, Muc4, Muc16 and Muc20, and of secreted Muc5ac and Muc5b was observed. Mucin gene expression increased during OM, peaking at 24 hours. High-secretory cells expressed the most mucin, including all six types, but all five epithelial types expressed some combination of mucins. Infection-related changes in DNA accessibility were observed for all six mucin genes. TFs with binding sites in these genomic regions, and which were up-regulated at 24 hours, were identified.

Discussion. Strong upregulation of mucin genes during OM by all epithelial cell types indicates less specialization for mucus production than might be expected from morphology. Changes in DNA accessibility during OM likely participate in up-regulating mucin gene expression, along with increased expression of TFs with exposed binding sites.

S10 L4

Otof gene transfer in DFNB9 mice carrying human founder non- truncating alleles

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Background

Gene therapy targeting otoferlin (OTOF) has emerged as a potential treatment for sensorineural hearing loss in DFNB9, where auditory nerve responses are severely impaired yet hair cells often remain viable. However, most preclinical efforts have focused on null alleles, leaving the efficacy of gene therapy for missense variants unresolved.

Materials and Methods

Using CRISPR/Cas9 mutagenesis, we generated mice carrying a human founder missense mutation (Otof p.R1934Q). These homozygous knock-in mice exhibited profound hearing loss but retained normal distortion product otoacoustic emissions (DPOAEs) for several months. We then designed a dual adeno-associated virus (AAV) system carrying the split murine Otof cDNA under a Myo15 promoter. The vectors were delivered unilaterally via the posterior semicircular canal in five-week-old mice. Auditory function was measured by auditory brainstem responses (ABRs) and DPOAEs, while immunofluorescence assessed inner hair cell transduction efficiency.

Results

Untreated Otofp.R1934Q/p.R1934Q mice showed negligible ABRs across tested frequencies but preserved DPOAEs, indicating hair cell integrity despite defective synaptic transmission. Four weeks after treatment, ABR thresholds in AAV-injected ears were substantially restored, approaching normal levels in animals with robust otoferlin expression. Wave I amplitudes remained somewhat diminished, but wave II amplitudes were near-normal, suggesting partial central compensation.

Conclusion

Our findings demonstrate that Otof gene transfer via a dual AAV approach can successfully rescue hearing in DFNB9 mice carrying a non-truncating founder variant. This highlights the therapeutic potential of gene therapy for missense OTOF mutations and suggests an extended window for intervention, given the stability of outer hair cells in this genotype.

S10 L5

Retraction of the tympanic membrane: is it an active self-defense mechanism? A new concept and its surgical implications against recurrency.

Karl- Bernd Hüttenbrink, Karl- Bernd Hüttenbrink

Background

The origin of a retraction pocket – what mechanism triggers the invagination of a healthy tympanic membrane skin - is still unclear. Today, there is convincing evidence that the retraction is not created by a negative pressure in the cavity due to some obscure tubal dysfunction. A new idea follows a biological principle of active self-healing on a local inflammation in a cavity: It is based on the capacity of the epidermis of the tympanic membrane with its immunologically active tissue to migrate horizontally. The skin advances into the cavity, makes contact and heals the underlying inflammation.

Methods:

Retrospective analysis of the interrelationship of a retraction pocket and underlying mucosa in 209 cholesteatoma - 2'nd look surgeries over the last decade.

Results:

A stable tympanic membrane over healthy aerated mucosa or a retraction pocket over granulation were described in 88.5%.

Conclusion:

The concept of the development of a retraction pocket due to a tubal dysfunction and negative pressure is outmoded today. A new idea interprets the retraction as a natural attempt to heal an underlying mucosal inflammation in the cavity. Similar biological phenomena exist, for example, in the migration of the omentum towards a local inflammation in the abdomen. This idea is compatible with all the different manifestations of retraction pockets and original or recurrent cholesteatoma. Some notes on the consequences for treatment and prophylaxis towards a recurrent cholesteatoma will be given.

S10 L6

Micro RNAs Implication in the Progression of Otitis Media

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Otitis Media (OM) is a ubiquitous condition of the middle ear characterized by acute infection mostly due to Non-typeable Haemophilus influenza (NTHi), progressing to chronic inflammation. Micro RNAs (miRNAs) are small RNA sequences carried in small vesicles for cell-to-cell communication, including trans-kingdom (bacterial to human), regulating gene expression. Our aim was to elucidate the role of human and bacterial miRNAs in OM progression.

Middle ear effusion (MEF) was collected from children undergoing myringotomy. A human middle ear cell line (HMEEC) was exposed to NTHi. Exosomes from both MEE and cell secretions were isolated, miRNAs purified with SeraMir kit and analyzed by Nanostring. HMEEC were transfected with miRNAs vs mimic and gene expression for MUC5B, MUC5AC and IL-8 was performed. The transcriptome was analyzed by mRNA-seq technique. miRNA transfection efficiency was evaluated by PCR and flow cytometry.

miR-378 was the most upregulated miRNA in HMEEC secretions in response to NTHi lysates and one of the most abundant in MEE. miR-378 transfection in HMEECs resulted in mRNA induction after 24hrs: mucins MUC5B 3.7-fold, MUC5AC 20-fold and IL-8 2-fold compared to negative control miRNA ($p<0.05$). As a potential mechanism of action, the mRNA-seq results showed miR-378 induces Wnt-1 pathway (3-fold, $p<0.0001$) and the downregulation of HIF1-α inhibitor (1.9-fold, $p<0.00001$) after 6hrs of incubation, pathways previously implicated in mucin regulation.

This study shows the mucogenic and inflammatory effect of miRNAs on the middle ear epithelium. Results will provide the groundwork to identify potential OM treatment strategies targeting miRNAs.

S11 L1

Can Hearing Aids Mitigate the Risk of Dementia in Older Adults with Hearing Loss?

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Background: Hearing loss has been associated with an increased risk of dementia. However, it is not known whether alleviation of hearing loss with hearing aids will mitigate the risk of dementia.

Materials and Methods: 573 088 persons, 50 years or older living in the region of Southern Denmark (298 006 women [52%]; mean [SD] age, 60.8 [11.3] years) with 23 023 cases of dementia were identified from the National Danish Register, the National Patient Register and the National Prescription Register. Patients with hearing loss were identified from a clinical database with audiograms as well as from the National Patient Register. Information about hearing aid acquisition was obtained from a database containing information about requested subsidy for a hearing aid purchase.

Results: Overall hearing loss was associated with an increased risk of dementia with an adjusted hazard ratio (HR) of 1.07 (95% CI, 1.04-1.11) compared with having no hearing loss. Out of 12060 cases of dementia, 3020 were hearing aid users and 1296 were not hearing aid users despite having a hearing loss. Hearing aid users had an increased risk of dementia with HR of 1.06 (95% CI, 1.01-1.10) whereas hearing aid non-users had an increased risk of dementia with HR of 1.20 (95% CI, 1.13-1.27).

Conclusion: Hearing loss was associated with dementia especially among those not using hearing aids. This suggests that the use of hearing aids may mitigate the risk of dementia in people with hearing loss.

S11 L2

A wide spectrum of rare causative genes identified by whole exome sequencing and phenotype similarity search in undiagnosed patients with syndromic hearing loss

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Background:

Several hundred syndromic disorders account for approximately 30% of the genetic causes of hearing loss. Because of such extreme heterogeneity, genetic diagnosis often goes undiagnosed for syndromic hearing loss with infrequent phenotypes. Sensitive and practical strategies need to be developed.

Materials and Methods:

Genetic causes of undiagnosed syndromic hearing loss were examined using a combination of whole exome sequencing (WES) and a phenotype similarity search system called PubCaseFinder in fifty-five families with syndromic hearing loss of unknown causes.

Results:

WES identified causative genes in 22 families, including both established genes associated with syndromic hearing loss (PTPN11, CHD7, KARS1, OPA1, DLX5, MITF, SOX10, MYO7A, and USH2A) and those associated with nonsyndromic hearing loss (STRC, EYA4, and KCNQ4). Among these, association of a coding variant of DLX5 with incomplete partition type I (IP-I) anomaly of the inner ear was identified for the first time in a patient. By using phenotype similarity search, COL1A1, CFAP52, and NSD1 were additionally identified as the causative genes. Furthermore, trio WES analysis identified ZBTB10 as a novel candidate gene for syndromic hearing loss with IP-I. A mouse model with a homozygous Zbtb10 frameshift variant resulted in embryonic lethality, suggesting the importance of this gene for embryonic development.

Conclusion:

WES analysis combined with phenotype similarity search revealed a wide spectrum of rare causative genes in patients with syndromic hearing loss, and is considered as a valuable approach for clinical genetic testing for undiagnosed syndromic hearing loss.

S11 L3

A Case of Michel Type Deformity in the Inner Ear Anomaly-Long Term Fellow Up of a Two-months-old Child to Age Twenty

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Background

In congenital deaf infants with hypoactive labyrinths, impairment of postural control in common and development of gross motor functions in the acquisition of head control and independent walking are delayed. The purpose of this study is to investigate balance and motor functions in a case with bilateral aplasia of labyrinth.

Material and Methods

A patient with Michel deformity in the inner ear anomaly has been followed up from 2 months old child to 20 years old.

Newborn hearing screening, ABR, CT scans and Brain MRI were conducted to evaluate inner ears and brain. Balance and motor functions were evaluated neurologically up to 20 years old.

Result

The temporal bone CT demonstrated bilateral aplasia of labyrinth. Primitive postural reflexes appeared well. However, head control at age of 6 months and independent walking at age of 2 years and 2 months were acquired so late. The postural balance function was instable before 6 years old but became possible to maintain thereafter. After the high school for deaf, he chose to be a professional wrestler. At age of 20, he does not show any problems of balance and motor functions.

Conclusion

In spite of bilateral aplasia of labyrinth, the patient's balance and motor functions are well acquired by central vestibular compensation until age of 20.

Figure shows Brain MRI (T1) at the level of auditory cortex (a) and cerebellum and brainstem (b) which demonstrated normal subcortical myelination in brain at age of 2 years.

S11 L4

Facial Nerve Stimulation in Otosclerosis Patients with Cochlear Implants – The Impact of Lateral versus Perimodiolar Electrode Array Positioning

Saku Sinkkonen, Joni Lindholm, Ville Sivonen

Background

Otosclerosis causes progressive conductive hearing loss and may progress to include sensorineural components. In advanced cases, cochlear implantation is an effective treatment, although in otosclerosis patients it may be associated with an increased risk of facial nerve stimulation (FNS). Structural and impedance changes in otosclerotic bone are potential contributors to this phenomenon. This study evaluates whether electrode array positioning — lateral wall versus perimodiolar — affects the incidence of FNS in this patient group.

Materials and Methods

This retrospective analysis included 57 otosclerosis patients (67 implants) treated at Helsinki University Hospital between 2004 and 2024 who underwent cochlear implantation due to otosclerosis-related hearing loss. Patients were grouped based on electrode array type, and the incidence of FNS was compared. The spread of intracochlear electric field was modeled. Results were further contextualized using data from prior original research.

Results

FNS occurred in 33% of patients with lateral wall electrode arrays, compared to 5.4% in those with perimodiolar arrays (OR 8.75, 95% CI 1.74–44.0; p = 0.0085). These findings align with previous studies, which also report significantly higher FNS rates with lateral wall arrays. Additionally, modeling of intracochlear electric field spread in otosclerotic bones supported these observations, highlighting the role of electrode positioning in neural stimulation patterns.

Conclusion

Electrode array positioning has a substantial impact on the risk of FNS in cochlear implant recipients with otosclerosis. Perimodiolar arrays are associated with a significantly lower risk and should be considered the preferred choice during surgical planning.

S11 L5

The role of vasculature of the internal auditory canal and functional surgery of vestibular schwannomaa

Elisabetta Zanoletti

Background

The rationale of functional microsurgery in vestibular schwannoma involves the attempt of hearing preservation surgery, hearing rehabilitation , and maximization of facial nerve preservation.

Early and proactive surgery is the benchmark of a curative and functional therapy.

The anatomy of the arteries running along the nerves in the internal auditory canal was explored and its role postulated in functional surgery.

Mat methods and results

A series of 130 temporal bone were dissected in laboratory, the vessels were coloured and silicon injected , stained with osmic acid, and their course along the nerves was studied with microsection or thick cleared section at the stereomicroscope.

Pictures and drawings of the findings are provided. The clinical impact of vasculature was explored in hearing preservation surgery and hearing rehabilitation with cochlear implants in vestibular schwannoma .

Conclusion

The role of vascular supply of the cochlear and facial nerve in VS was investigated and findings were reported.

In relation to the results of our most recent surgical series of vestibular schwannoma, the dissection findings were associated to the functional outcome of early proactive surgery.

S12 L1

Bio-sensing for cochlear implant-induced trauma: new developments

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Background: Insertion of a cochlear implant (CI) electrode array could induce trauma to the fragile cochlear microstructures. Advancements in electrode design, electrophysiological monitoring, robotic-assisted insertion, and intracochlear drug delivery have reduced trauma. However, little is known on the release of inflammation markers during insertion. Implantable hydrogen peroxide sensors could address this issue since hydrogen peroxide is linked to acute and chronic inflammation.

M&M: CI electrode array modifications included electrodeposition of iridium oxide (IrOx) as a quasi-reference electrode, a poly(o-phenylenediamine) permselective membrane, and a sulfobetaine antifouling layer to improve selectivity and prevent biofouling. These modifications were characterized on microfabricated platinum test electrodes, showing stable IrOx potentials for 28 days in artificial perilymph and resistance to macrophage and fibroblast adhesion. The sensors demonstrated a peroxide detection limit of 2.5 μM in vitro. In a CI gerbil model, we inserted the modified electrode array through the round window. Trauma was assessed with a microscopic-based optical coherence tomography system and contrast-enhanced micro-CT scans.

Results: In vivo testing in a gerbil model showed elevated hydrogen peroxide levels (from 61 ± 4 μM to 114 ± 8 μM) following insertion trauma. While IrOx was stable in vitro, it showed a 40 mV drift over 6 hours in vivo. Using an external reference electrode we were able to measure for the first time the peroxide concentration in the cochlea.

Conclusion: the potential of using CI electrode arrays to monitor implantation-induced trauma and inflammation is highlighted. Potential translation to the clinic will be discussed.

S12 L2

Variable inner ear pressure changes associated with manual electrode insertion; a temporal bone study

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Background: Cochlear implantation (CI) can induce inner ear pressure fluctuations, potentially compromising residual hearing—a critical concern for hybrid CI users. Previous studies report conflicting findings on pressure changes during electrode insertion. This study systematically evaluated intracochlear pressure dynamics during electrode insertion in a cadaveric model.

Methods: Seven fresh-frozen human temporal bones underwent mastoidectomy and posterior tympanotomy to expose the round window. A 1.0 mm fenestration was created in the semicircular canal for fiber-optic pressure sensor placement. Following round window membrane perforation, a Cochlear™ Nucleus® electrode was inserted over 10 seconds while continuously monitoring pressure changes.

Results: Among 72 insertion trials, 19 measurements (26%) across 3 specimens demonstrated detectable pressure increases, with a maximal elevation of 1.5 dB SPL. The majority (74%) showed no significant pressure variation.

Conclusions: Manual CI electrode insertion generates only marginal intracochlear pressure changes in this experimental model. The observed pressure elevations (≤1.5 dB SPL) appear physiologically insignificant, suggesting minimal risk to residual hearing from this mechanism. These findings support the mechanical safety of conventional CI insertion techniques regarding pressure-related effects.

S12 L3

A Novel Surgical Technique in Bilateral Cochlear Implantation

Kadir Serkan Orhan

Background

Bilateral cochlear implantation is a well-established method for restoring binaural hearing in individuals with severe to profound sensorineural hearing loss. This study introduces a novel surgical technique aimed at improving the efficiency and safety of bilateral cochlear implantation.

Materials and Methods

A prospective study was conducted on 30 patients who underwent bilateral cochlear implantation using the new approach. Intraoperative metrics, including total surgical time and complications, were recorded.

Surgical Technique

After antiseptic preparation with povidone-iodine and full facial draping, surgery began on one ear. A postauricular incision was made, followed by creation of a subperiosteal pocket. Mastoidectomy and posterior tympanotomy were performed, exposing the round window niche. The procedure was paused, and the head was rotated to the contralateral side.

The same steps were repeated on the second ear, including full exposure of the round window membrane. The receiver-stimulator was placed in the subperiosteal pocket, and the electrode array was inserted into the scala tympani via the round window. Intraoperative electrophysiological testing was performed, and the incision was closed in layers.

The head was then rotated back, and the procedure was completed on the initial ear in the same manner.

Results

The novel technique significantly reduced operative time compared to standard methods. No major intraoperative or postoperative complications were observed.

Conclusion

This prospective study suggests that the new bilateral cochlear implantation technique improves surgical efficiency without compromising patient safety or clinical outcomes.

S12 L4

MATURATION OF FREQUENCY RESOLUTION IN INFANTS WHO USE COCHLEAR IMPLANTS

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Background: The lack of clinical tools to assess suprathreshold auditory acuity in hearing-impaired infants limits early, individualized optimization of auditory input via a cochlear implant (CI). Frequency resolution (FR), which matures during infancy in normal-hearing (NH) children, correlates with speech understanding in prelingually-implanted CI users. This study examined FR development in infants with CIs, hypothesizing that FR matures by six months post-activation.

Methods: Nine infants with CIs (implanted by 18 months, no neurocognitive diagnoses or severe cochlear malformations) and 11 post-lingually implanted adults (established CI users) were tested. FR was measured as the highest ripple density (ripples per octave, RPO) distinguishable from 20 RPO. Modulation depth was fixed at twice each listener's spectral modulation sensitivity (SMS) threshold—the smallest depth needed to discriminate 0.5 from 20 RPO. Thresholds were obtained using a single-interval observer-based psychoacoustic procedure with stimuli presented at 70 dBA in sound-field to listeners using one CI in their preferred ear. Linear mixed-models assessed the effects of hearing age (3 months, 6 months, adult) on SMS and FR.

Results: SMS improved significantly with hearing age, from 3 to 6 months and from 6 months to adulthood. In contrast, no effect of age was observed for FR—infants performed at adult-like levels as early as 3 months post-activation.

Conclusions: Findings suggest early maturation of FR and slower development of SMS in CI users, mirroring patterns in NH children. FR may serve as a valuable clinical tool for assessing auditory function and optimizing cochlear implant outcomes in infants.

S12 L5

Acoustic Hearing Preservation Manual vs Robotic Cochlear Implant Insertion: Rates of Long-Term Delayed Hearing Loss

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Objective(s): Combining acoustic hearing with electrical processing has advantages over electrical processing only. Robotic assisted CI insertion is one strategy that could preserve residual acoustic hearing. There are concerns of progressive hearing loss in this population. The purpose of this study is to investigate whether robotic-assisted CI insertion reduces delayed-onset hearing loss (DOHL).

Methods: 89 subjects with residual low frequency hearing and a LPTA (< 70dB HL) received either MedEl (ME)Flex N=46 (Manual N=30; Robotic N=16) or Advanced Bionics (AB) N=43 (Manual N=30; Robotic N=13). iotaSOFTTM robotic system was used for robotic insertion. DOHL is defined as more than a 10 dB decrease in LFTA within the first year.

Results: At initial activation (IA) functional acoustic hearing was maintained in 79% (70/89) of subjects. Following IA for up to 1-year, The ME manual group had 5 subjects (22%) with DOHL and robot= 0%. The AB manual group had 6 subjects (40%) with robot 0 subjects experienced DOHL. Combining subjects from AB and ME, the manual group had a total of 11 (29%) subjects with DOHL, compared to 0 subjects (0%) DOHL with the robot . (Fisher's exact test, two-tailed, p = 0.0108).

Conclusion: Robotic-assisted electrode insertion is associated with improved hearing preservation over 1 year following activation compared manual insertion. Surgical insertion of a cochlear implant manual or robotic carries a risk of loss of immediate functional hearing of 21% in our population. Robotic insertion significantly reduces the risk of DOHL.

S12 L6

Adult Simultaneous Cochlear Implantation: Local Anesthesia

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Purpose: Cochlear implant (CI) surgery is conventionally done under general anesthesia (GA). However, many patients are unable to undergo GA due to various reasons, raising the need for an alternative safe option. CI under local anesthesia is feasible and safely done in patients who can't tolerate GA. This approach allows for device fitting immediately after surgery. This study aims to evaluate simultaneous bilateral cochlear implant (BiCI) surgery performed under local anesthesia with sedation in adults. To our knowledge, this is the largest cohort of patients who underwent this approach. Methods: This is a retrospective chart review in a tertiary center. We included all adult patients who underwent simultaneous BiCI under local anesthesia with sedation from 2018 to 2024. The feasibility of BiCI under local anesthesia with sedation was assessed through clinical, surgical, audiological, and patient questionnaire data. Results: Six patients underwent simultaneous BiCI with local anesthetic and sedation. Mean age was 41.7 ± 16.0, comprising 66.7% male and 33.3% female. No intraoperative problems were encountered. All woke up from sedation without any agitation or difficulties. Their recovery was uneventful. No dizziness, nausea, or vomiting were reported. The device was activated immediately postoperatively. Pure tone audiometry, speech reception threshold, and word recognition score were significantly improved. Positive experiences were reported in all patients. Conclusion: Bilateral simultaneous cochlear implantation under local anesthesia in adults is achievable, through a multidisciplinary approach. This approach is a potential alternative option for some patients and could optimize their hearing rehabilitation.

S12 L7

Beyond the curtains of Non-syndromic Hereditary Hearing Loss (NSHHL): Whole Exome Sequencing (WES) reveals the presence of Non-Syndromic Mimics (NSMs)

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Background: NSHHL entangled genetic bases can be complicated by peculiar and understudied clinical conditions, namely NSMs.

Methods: In the last 18 months, 83 patients, apparently affected by NSHHL underwent WES. Whenever a NSM was identified, reverse phenotyping was performed to assess whether the subject already presented extremely subtle syndromic features or if additional characteristics were expected to develop in the future.

Results: WES highlighted a molecular diagnosis in 44.6% of patients (37/83 cases) and 14 NSMs were identified. NSMs were classified as follows: 1) five patients already presenting subtle syndromic features that were missed during the clinical evaluation and 2) nine subjects that are expected to develop additional clinical features later in life. In Group 1, four patients resulted to be carriers of variants within genes associated with autosomal dominant conditions, namely GATA3, NLRP3, ACTG1, and MITF while one patient harboured a homozygous variant within the BCS1L gene, associated with an extremely rare mitochondrial disorder. All Group 2 patients were affected by Usher syndrome: seven patients were carriers of biallelic variants within the USH2A gene, one patient presented two compound heterozygous variants in the CDH23 gene, and one subject harboured a homozygous variant in the USH1C gene.

Conclusions: NSMs have been identified in 37.8% of all NSHHL solved cases, thus representing an unexpectedly frequent occurrence. These findings underline how apparently NSHHL patients need to be carefully evaluated by a multidisciplinary team involving a medical geneticist to provide a tailored management plan and timely identify additional clinical issues.

S12 L9

UPDATE IN ROBOTIC COCHLEAR IMPLANTATION - HEARO & OTODRIVE

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In 2005 Marco Caversaccio started the project of Robotic Cochlear Implantation. Since then the author is actively involved into the program. Until 2010 the project was financed by the Swiss Scientific National Fund. Over the years a stable, complex, reliable, safe and accurate system could be built.

After 2010 a cooperation in between MEDEL (Austria) and CASCINATION (Switzerland) was started.

The name of this new Cochlear Implant Robot is HEARO.

Prof. Caversaccio and his team did the worlds first surgeries, followed by Vienna as 3rd department worldwide. Together we performed > 90 successful robotic cochlear implant surgeries in adults.

All surgeries are planed by Otoplan System. Once the Otoplan setting is done, the surgeon observes the surgery performed by the HEARO Robot.

We show and report about the first 90 consecutive cases and the experience from the HEARO study team.

The HEARO CI Robot is a step into the future and proves that safe CI surgery already can be performed by a robot.

The accuracy of the system is 0,01mm. Nevertheless the surgery is still observed by a surgeon.

Since November 2024 we combined the HEARO system with the fully automatic electrode insertion system OTODRIVE/OTOARM.

The OTODRIVE implants the electrode array automatically into the Scala Tympany. OTODRIVE can be used without the HEARO as “stand-alone” tool together with the OTOARM. We will report about our first 30 Otodrive surgeries.

Keywords: Robotic, Cochlear Implant

The author is since 2005 member of the HEARO study group and co-originator of Otoplan and Otodrive.

S12 L10

GABA inhibition in humans with tinnitus

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Background

Tinnitus is presumably related to enhanced spontaneous activity in the auditory cortex. Experiments in animals have suggested that this may be due to deficient GABAergic inhibition. Magnetic resonance spectroscopy in humans showed evidence for reduced GABA concentration in the auditory cortex. We further investigated the role of GABA by imaging GABA receptors in a positron emission tomography (PET) scanner.

Materials and Methods

Flumazenil PET scans were conducted in three subject groups: (1) normal hearing controls without tinnitus, (2) participants with moderate sensory neural hearing, (3) participants with moderate hearing loss and additional tinnitus. PET scans were analyzed in order to obtain a measure of the binding potential (BP), which is a function of the density of GABA receptors and of their binding properties.

Results

The BP was clearly enhanced in the auditory cortex in participants with tinnitus and hearing loss, as compared to participants with hearing loss only. This differences did not depend on hearing loss, age, and measures of hyperacusis, anxiety and depression.

Conclusion

The enhanced binding potential indicates either an upregulation of GABA receptors in the auditory cortex, or a change of their binding properties. These may be compensatory mechanisms in the brain to counteract hyperactivity. The results provide clear clinical evidence for a critical role of GABAergic inhibition in tinnitus, which may be a basis for objective diagnosis of tinnitus. Moreover, these results strongly motivate re-evaluation of pharmaceutical interventions in order to silence tinnitus by enhancing GABAergic inhibition.

S13 L1

Innovations in the Management of Unilateral Vocal Fold Paralysis: Expanding Therapeutic Possibilities

Ihab Atallah

Background

Unilateral vocal fold paralysis (UVFP) significantly affects phonation, swallowing, and breathing, often necessitating intervention to restore both voice and airway function. While traditional management has required a trade-off between these priorities, recent advancements in reconstructive transoral laser microsurgery (R-TLM) have introduced novel techniques that expand treatment possibilities. This presentation provides an overview of both established and emerging approaches that redefine UVFP management.

Materials and Methods

Surgical techniques reviewed include medialization thyroplasty, augmentation procedures, arytenoid repositioning, lateralization, and laryngeal reinnervation. The introduction of R-TLM has refined transoral medialization, novel arytenoidopexy techniques, and vocal fold lateralization procedures. Additionally, certain interventions can be performed under local anesthesia, providing an alternative therapeutic option for select patients. A key focus is augmentation-lateralization, a hybrid technique designed to enhance posterior glottic function while preserving phonatory integrity. A symptom-driven clinical evaluation framework is also presented to emphasize individualized treatment selection based on patient-specific impairments.

Results

The integration of R-TLM in UVFP treatment has significantly expanded available interventions. Augmentation-lateralization, alongside other transoral microsurgical techniques, allows for a more precise balance between voice restoration and airway optimization. A refined clinical assessment approach further enhances therapeutic decision-making, aligning interventions with patient-specific symptoms.

Conclusion

The treatment paradigm for UVFP is shifting beyond conventional approaches. Advances in R-TLM, augmentation-lateralization, and tailored evaluation strategies are transforming laryngeal surgery, offering new solutions that optimize both phonation and respiration. This presentation bridges established methods with emerging innovations, demonstrating how modern techniques are reshaping the future of UVFP management.

S13 L2

Novel surgical approach to address posterior glottic stenosis

Miroslav Tedla, Bálint Tóth, Korim Žofia

The report describes cases of two patients with stenosis in the area of the posterior glottic commissure. Our chosen surgical solution was a novel previously unpublished procedure using a silicone stent inserted and sewn into the tunnel in the area of the stenosis. The silicone stent was removed after 6 weeks which allowed sufficient healing time for the most posterior part of the stenosis, and the remaining part of the stenosis was interrupted. The surgical procedure led to removal of the tracheostomy tube, breathing and voice improvement and increased the quality of life. This treatment method appears to be a suitable way of solving some types of stenosis in the area of the posterior glottic commissure.

S13 L3

Establishment of humanized mouse models in the evaluation of PD-1/PD-L1-axis blockade-based head and neck cancer immunotherapy

Yoon Se Lee, Sang Yoon Kim

Background

Immunotherapy has emerged as a promising treatment option in head and neck cancer, spanning initial to salvage settings for recurrent or metastatic disease. However, only a limited subset of patients—particularly those with advanced disease—respond to immune checkpoint inhibitors targeting the PD-1/PD-L1 axis. While immunocompetent mouse models have been widely used to study treatment responses and underlying mechanisms, significant interspecies differences in genetics and immune systems have limited their translational relevance. To address this, humanized mouse models with reconstituted human immune systems have been developed for preclinical studies. This study aimed to establish a humanized xenograft model of head and neck cancer using human peripheral blood mononuclear cells (PBMCs) and to evaluate its applicability for testing PD-L1-targeted therapies.

Methods

NOD-scid-IL2Rg-/- (NSI) mice were injected with human PBMCs via tail vein. The engraftment of human T cells was confirmed by flow cytometry for CD3 and CD45 markers. A human head and neck cancer cell line, PCI-13, was selected based on PD-L1 expression via Western blotting. After establishing a cell-derived xenograft (CDX) model, mice were treated with a human anti-PD-L1 antibody, and tumor growth was monitored.

Results

Humanized NSI mice showed successful T-cell engraftment and supported tumor growth of PCI-13 cells. Treatment with anti-PD-L1 resulted in delayed tumor progression compared to untreated controls.

Conclusion

The human PBMC-derived CDX model is feasible and effective for evaluating PD-L1-targeted therapies. This model may serve as a valuable preclinical platform to predict therapeutic responses in head and neck cancer immunotherapy

S13 L4

E-cadherin-deficient epithelium creates a leaky barrier and promotes fibrosis in idiopathic subglottic stenosis

Alexander Hillel

Background: Idiopathic subglottic stenosis (iSGS) is a rare disease of the upper airway characterized by pathologic narrowing of the subglottis. Due to the need for repeated surgical treatment, patient and provider satisfaction with surgical therapy has historically been low. To address this unmet need, an innovative endoscopic surgery was developed that resects the stenosis and replaces diseased mucosa with a healthy epithelial graft, providing durable outcomes. This successful surgery that replaces the epithelium suggests that epithelial barrier dysfunction could be the underlying cellular abnormality that instigates the fibroinflammatory cascade and phenotypic fibrosis in iSGS.

Methods: We designed a series of experiments to assess the role of epithelial barrier dysfunction in iSGS. Single-cell RNA sequencing and protein assays of iSGS patient specimens was compared with normal controls to identify candidate genes leading to the observed epithelial barrier dysfunction. Subsequent mechanistic studies were performed in a genetically-altered murine SGS model with selective deletion of E-cadherin (CDH-/-) in airway mucosa.

Results: The most highly differentially expressed gene was E-cadherin, and protein assays confirmed a reduction in this barrier protein and in iSGS epithelial permeability. CDH-/- mice with SGS had increased fibrosis and greater mortality compared to wild-type controls.

Conclusion: These results support a “leaky barrier” hypothesis for iSGS where luminal antigens enter the immune□naïve subglottic lamina propria through permissive E-cadherin-deficient epithelium, triggering a fibroinflammatory cascade and the development of subepithelial fibrosis. Improving E-cadherin abundance and epithelial barrier function may be a targeted therapeutic strategy for iSGS and other more common fibrotic airway diseases.

S13 L5

Outcomes of Bilateral Hypoglossal Nerve Stimulation for Treatment of Sleep Apnea

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Background: Obstructive Sleep Apnea (OSA) is a prevalent and heterogeneous condition associated with comorbidities. Continuous positive airway pressure (CPAP) therapy is not always effective or tolerated. Bilateral hypoglossal nerve stimulation (bHNS) has emerged as a promising alternative treatment offering a minimally invasive approach.

Results: Several studies have demonstrated the effectiveness of implantable bHNS system in controlling OSA. Most recent multicenter, prospective DREAM clinical trial data became available. A total of 115 patients with moderate to severe OSA were enrolled. Inclusion criteria were Apnea-Hypopnea Index (AHI) ≥15 events/hour and a Body Mass Index (BMI) 18 to 32 kg/m². At baseline, the cohort had a mean AHI of 28.0 events/hour, mean ODI of 27.0 events/hour, and mean BMI of 28.5 kg/m². At 12 months, 73 patients (63.5%) achieved the AHI responder criterion, and 82 patients (71.3%) met the ODI responder criterion. The median reduction in AHI was 70.8%, with similar improvements observed in both supine and non-supine sleep positions. Significant improvements of the Functional Outcomes of Sleep Questionnaire (FOSQ) score and the Epworth Sleepiness Scale (ESS) were also achieved. During the trial11 serious adverse events (SAEs) were reported resulting in an SAE rate of 8.7%, three SAEs were device-related, and 3 patients underwent device explantation.

Conclusions: bHNS therapy demonstrated significant AHI and ODI reduction, and improvements in sleep quality and daytime sleepiness over a 12-month period with low rate of serious adverse events supporting a viable treatment option for patients with moderate to severe OSA.

S13 L6

The Effect of Hypoglossal Nerve Stimulation on Sleep Apnea Specific Hypoxic Burden in patients with Obstructive Sleep Apnea

Olivier M VANDERVEKEN

The apnea-hypopnea index (AHI), which is the primary metric used for diagnosis and management of obstructive sleep apnea (OSA), has important limitations. Recently, sleep apnea specific hypoxic burden (SASHB) was introduced as a novel metric to assess OSA severity, characterizing respiratory event-related depth, duration and frequency of oxygen desaturations. The aim of this study was to investigate the 1-year effect of hypoglossal nerve stimulation (HGNS) therapy on SASHB.

Twenty-five patients implanted with a respiration-synchronized HGNS device were included in this study. All patients underwent a baseline and 1-year follow-up polysomnography. An SASHB ≥ 60 %min/h was used as the threshold, previously shown to be associated with increased cardiovascular/mortality risk in observational studies.

HGNS therapy significantly reduced SASHB from 51.5 [30.9-84.8] at baseline to 11.6 [5.1-24.5] %min/h at 1-year post-implantation ($p < 0.001$), corresponding with a 76 [47-90] % reduction in SASHB. In 8 out of 9 patients with a baseline SASHB ≥ 60 %min/h, SASHB decreased to below this threshold at 1-year post-implantation. The reduction in AHI was 68 [51-87] % from 29.6 [20.7-39.7] at baseline to 8.3 [4.1-13.5] events/h at 1-year post-implantation ($p < 0.001$) with 76% of the patients meeting Sher15 responder criteria.

The findings of this proof-of-concept study showed that HGNS therapy significantly reduces both SASHB and AHI. One-year post-implantation, 96% of patients had an SASHB below 60%min/h, which is associated with reduced cardiovascular risk.

S14 L2

Impact of Management Decisions on Outcomes of Paediatric Subperiosteal Orbital Abscess: A Retrospective Study

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[1] Royal Childrens Hospital Melbourne

Background: Subperiosteal orbital abscess (SPOA) is a serious complication of paediatric orbital cellulitis that is variably managed with surgical drainage in addition to antibiotics and nasal therapeutics. The literature reports significant variation in the rates and timing of surgical intervention in these patients, and the impact on patient outcomes is unclear.

Methods: Retrospective cohort study (2015–2025) at The Royal Children's Hospital in Melbourne, Australia, of children diagnosed with sinusitis-related SPOA. Patients were stratified by management type (surgical versus non-surgical) and by timing of surgical intervention relative to hospital admission (< 48 hours versus >48 hours). The primary outcomes were hospital length of stay (LOS) and complication rates.

Results: 118 paediatric SPOA patients were identified. Of these 70 (59%) underwent surgical management and 48 (41% were managed non-surgically). Surgical intervention was delayed for longer than 48 hours in 29 patients. Surgical management was associated with a significantly longer mean LOS compared to medically managed patients. However, surgery performed within 48-hours of admission resulted in significantly shorter LOS compared to surgery after 48 hours. There was no significant difference in complication rates between surgical and non-surgical groups.

Conclusion: There was significant variation in the modality and timing of patient management. While complication rates were similar between groups, non-surgical and early surgical (<48 hours) patients were able to be discharged earlier. Future studies should aim to improve the stratification of SPOA patients to better predict surgical need, such as by investigating radiologic factors (infection/abscess size, location, and complications), to optimise outcomes.

S14 L3

Nasal Dilators in Sports Activities – Magic or Gimmick?

Per Gisle Djupesland, Per Gisle Djupesland

Background:

Nasal dilators (ND), external and internal, expand the flow-limiting nasal valve to enhance nasal airflow and prevent inspiratory nasal collapse. In subjects with rhinitis and septal deviations, ND may reduce snoring, mouth-breathing and sleep disturbances. ND are not included in the World Anti-Doping Agency (WADA) list, and hence commonly used by high-level athletes with the intent to improve performance. The purpose of the presentation is to review the literature on the effects of ND during physical exercise.

Materials and Methods:

Results from two recent meta-analyses, including controlled trials with ND in healthy individuals during running and other forms of physical exercise, are presented. Key parameters are maximal oxygen consumption (VO2max), heart rate (HR) and rating of perceived exertion (RPE).

Results:

The most recent meta-analysis showed statistically significant increase in VO2max and RPE during running with ND when compared to placebo, but not when compared to controls (Gomes 2022). The included studies are small, and the evidence has very low certainty. Another recent meta-analysis including various forms of physical exercise showed no significant improvement of ND in VO2max, HR or RPE outcomes (Dinardi 2021). Related studies, including published work by the author (Djupesland 2001), offering potential explanations of the conflicting results of ND, are presented.

Conclusions:

While ND increases nasal dimensions and nasal airflow, the current evidence of effects on physical exercise is conflicting and with very low certainty. To some athletes ND may offer true magic and to others ND may represent a permitted gimmick with potential placebo effects.

S14 L4 WITHDRAWN

Transnasal transsphenoidal endoscopic pituitary adenoma surgery: Prospective study on patients' Anterior Skull Base-12 (ASK-12) scores

Karol Silla[1], Abdullah Illeyan[2], Ahmed Shaikh[1], Emad Al-Duhirat[1], Hamad Alsaey[1], Mansour Alsulaiti[1], Mashael Alhail[1], Sara Ashkanani[1], Sirajeddin Belkhair[2], Ghanem Al Sulaiti[2], Ahmed Own[2], Shanmugam Ganesan[1]

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Background: The transnasal endoscopic approach for pituitary adenomas has risk for sinonasal complications. Our study investigated the trend in Anterior Skull Base Nasal Inventory-12 (ASK-12) scores for such patients from pre-op to post-op with long-term follow up.

Methods: 67 patients who underwent primary transnasal transsphenoidal endoscopic approach pituitary adenoma surgery at a single tertiary center in Qatar were prospectively followed from 2021 to 2024. ASK-12 questionnaires pre-operatively and post-operatively (2 weeks, 3 months and 1 year) were administered.

Results: There was significant increase in overall mean ASK-12 scores from pre-op to post-op week 2 ($p < 0.05$) with a mean 65.66% increase from baseline. Post-op week 2 mean ASK-12 score declined at post-op month 3 ($p<0.05$). Mean difference between post-op month 3 and post-op year 1 ASK-12 scores was insignificant ($p=0.31$). Among four chosen ASK-12 symptoms (loss of smell, breathing difficulty, nasal discharge, and headache), loss of smell ranked most debilitating at post-op week 2. Five patients had severe septal deviating requiring concomitant septoplasty and they had decreased mean ASK-12 scores during 3-month and 1-year follow up (effect size -0.431 and -1.088 respectively) compared to patients who didn't undergo septoplasty.

Conclusion: Patients undergoing transnasal transsphenoidal endoscopic approach pituitary resection may be counselled on transient worsening of rhinological outcomes—especially loss of smell—at week 2 then marked improvement at month 3 until year 1 after surgery. Furthermore, septoplasty may also be considered for patients requiring better pituitary access as sinonasal outcomes improve with better chances of surgical outcomes.

S14 L5

A Comprehensive Analysis of Big Data on Health Observations Concerning Cedar Pollinosis Among Youth in Fukui, Japan

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Objective: The incidence of cedar pollinosis is escalating rapidly, particularly among individuals aged 5-9 years, necessitating urgent countermeasures. During the COVID-19 pandemic, new lifestyle habits emerged, including the widespread use of masks by both children and adults when outdoors. Surveys conducted during this period indicated a reduction in new cases of cedar pollinosis to less than half. This study aims to collaborate with medical and educational institutions to survey cedar pollinosis symptoms among elementary and junior high school students using an application, and to analyze the resulting data to aid in preventing new onset and severe cases.

Method: Under the government's GIGA School Initiative, an environment was established to enhance ICT education, providing each student with a tablet PC. Utilizing this infrastructure, an application developed by the University of Fukui was implemented for daily health management. Approximately 1,000 students from three elementary and junior high schools in Fukui Prefecture participated in the program. Students recorded information on their nasal symptoms using the provided devices from February to April 2025, excluding school holidays.

Results: Participants recorded data on nasal symptoms, itchy eyes, drowsiness with their severity, and mask usage at school as part of their daily school activities. It is hypothesized that mask-wearing during the cedar pollen dispersal period, even post-pandemic, will mitigate the rise in cedar pollinosis among children. This study was conducted to establish a framework for promoting this practice. Issues related to a collaborative platform between medicine and education for joint research on children's health will be identified.

S14 L6

Periorbital suspension and the role of anterior ethmoidal artery during endonasal endoscopic access to the lateral frontal sinus and skull base

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Endonasal endoscopic approaches (EEA) to the frontal sinus face significant limitations, particularly in accessing the lateral frontal sinus and adjacent skull base regions. This challenge is heightened in cases of well-pneumatized frontal sinuses, where the standard EEA may be inadequate, often necessitating external approaches involving skin incisions and osteoplastic techniques. Despite advancements in endoscopic techniques, anatomical studies have consistently demonstrated limited or no access to the lateral frontal sinus through traditional EEA. Periorbital suspension technique, earlier presented by us, offers a potential solution by enhancing lateral access. Since the anterior ethmoidal artery (AEA) appears to influence the feasibility of this technique, we conducted an anatomical study to evaluate its role in expanding EEA reach.

Ten cadaver heads (20 sides) underwent pre-dissection CT evaluation to assess frontal sinus and supraorbital recess pneumatization. Gradual dissections were performed in the sequence of Draf I, IIA, IIB, and III procedures, measuring visual and instrumental access to the lateral frontal sinus, skull base, and supraorbital recess. These measurements were repeated after AEA transection and application of the periorbital suspension technique.

Our findings revealed that the medial orbital wall limits lateral access, even with extensive Draf procedures. However, AEA transection allowed sufficient lateralization of the periorbita, enabling effective periorbital suspension. This maneuver facilitated complete access to the lateral frontal sinus and surrounding areas in all specimens.

In conclusion, the AEA is a key anatomical structure in enabling successful periorbital suspension. Its transection significantly enhances lateral reach in EEA, offering a valuable extension to current surgical approaches.

S14 L7

Clinical and Proteomic Analysis of Biologic Treatments in CRSwNP: Real-World Insights from a Belgian Cohort

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Background: Chronic rhinosinusitis with nasal polyps (CRSwNP) is a type 2 inflammatory condition increasingly managed with biologic therapies such as Omalizumab, Mepolizumab, and Dupilumab. Real-world clinical outcomes, supported by molecular profiling, are essential to guide personalized treatment strategies.

Methods: Clinical and molecular data were collected from 129 patients with CRSwNP treated with Omalizumab (n=35), Mepolizumab (n=65), or Dupilumab (n=28). Clinical outcomes were assessed at baseline and after 12 months using the Total Nasal Polyp Score (TNPS), SNOT-22, UPSIT smell test, Asthma Control Test (ACT), and a visual analogue scale (VAS) for smell. Proteomic profiling of nasal secretions was performed using high-resolution mass spectrometry. In addition, sinonasal tissue biopsies from selected patients were analyzed for eosinophilic and neutrophilic inflammation via immunohistochemistry and single-cell RNA sequencing.

Results: All three biologic therapies led to significant improvements in TNPS, UPSIT, VAS smell, and SNOT-22 scores, with the most pronounced improvement in SNOT-22 observed in the Mepolizumab and Dupilumab groups. Proteomic analysis identified 52,618 precursor peptides and 5,075 protein groups, of which 4,086 were reliably quantified (≥15 valid LFQ values in at least one condition). Biologic treatment was associated with a downregulation of eosinophilic inflammation and a minimal increase in neutrophilic activity.

Conclusion: Biologic therapies offer substantial clinical benefit in CRSwNP and induce distinct molecular changes in sinonasal inflammation. Nasal secretions represent a promising non-invasive tool for monitoring biologic treatment responses at the mucosal level.

S14 L8

Salivary cortisol concentration is an objective measure of the physiological response to acute stress caused by loud music

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Purpose: This study aims to examine the potential associations between salivary cortisol concentrations and subjective stress test scores in healthy individuals subjected to sound-related, psychological, and physical stressors.

Methods: A single-center observational cross-sectional design, with a sample size of 36 subjects recruited from a tertiary referral audiology center. Between 2023 and 2024, the study recruited subjects with normal hearing, baseline salivary cortisol levels, and subjective stress levels. The participants were requested to complete an STAI-Y1 questionnaire and provide salivary cortisol samples before and following exposure to sound-related, psychological, and physical stress tests.

Results: Exposure to psychological and physical stressors significantly increased STAI-Y1 scores (Friedman's test, $\chi2 = 57.118$, df =2, p=0.377). This increase was greater than that observed in response to loud, favorite music (Friedman's test, $\chi2 = 57.118$, df =2, $p<0.0001$). The salivary cortisol concentration significantly increased in all three provocation tests (Friedman's test, $\chi2 = 95.264$, df =5, $p<0.0001$). Furthermore, there is no significant difference in salivary cortisol concentrations between the three pre-test and post-test measurement intervals, indicating a comparable stress-inducing pattern regardless of the nature of the stimulus (Friedman's test, $\chi2 = 95.264$, df =5, $p>0.05$).

Conclusions: Exposure to loud favorite music increases salivary cortisol concentrations, as does acute physical and psychological stress. Interestingly, unlike psychological and physical stress, loud music was not objectively perceived as stress, which may mask the physiological signs of stress, potentially increasing the risk of both acute and chronic stress-related health outcomes.

S14 L9

Skull Vibration Induced afternystagmus - a new clinical indicator of anterior canal dehiscence.

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Background

Vibrations applied to the cranium induce, in up to 92% of patients with CT-verified anterior canal dehiscence (ACD), a perstimulatory nystagmus most often ipsilaterally beating when the vertex location is stimulated at 100 Hz. The skull vibration-induced nystagmus test is a bone-conducted Tullio phenomenon in patients with a 3rd mobile window syndrome.

Material and methods

A prospective series of 43 CT-verified ACD patients [33 unilateral ACD (uACD) and 10 bilateral ACD (bACD)] was compared with a series of 43 controls. The SVINT was performed at 100 Hz on each mastoid and vertex for 5 s in a patient with head upright and vision denied. In a second step, a longer stimulation duration of >10 is performed, which is more likely to observe a specific afternystagmus (AN).

Results

A skull vibration induced afternystagmus is characterized by a persistent nystagmus with a slow decay after stimulation withdrawal and is associated with dizziness.

Twenty four out of 43 patients (56 %) with ACD stimulated at 100 Hz by bone-conducted vibrations showed an AN. Such an AN was not observed in controls stimulated at high frequencies.

Conclusion

An afternystagmus is described for the first time in ACD when a sufficiently long duration stimulation is performed with BCV. The AN, as the perstimulatory SVIN, is beating ipsilaterally toward the side with hearing symptoms when the vertex is stimulated. The vertex is the optimal location for obtaining AN and is a reference location for indicating the skull vibration-induced nystagmus direction in the ACD.

S14 L10

Gaze Position Error During Head Impulses as a Predictor of Symptom Severity in Subacute Dizzy Patients

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Objective:

This study aimed to evaluate the clinical relevance of gaze position error (GPE) following rapid head movements in relation to symptom recovery in patients with acute unilateral vestibulopathy (AUVP).

Methods:

A total of 26 patients diagnosed with AUVP and 48 age-matched healthy controls were enrolled. All participants underwent the video head impulse test (vHIT) during the acute phase, with a follow-up vHIT performed 30 days post-symptom onset. Symptom burden and impact on daily life were assessed using the Dizziness Handicap Inventory (DHI).

Results:

Based on normative control data, a GPE threshold of 4° was determined as the cut-off for abnormality. The mean DHI score among patients was 26.7 (±28.9 SD), with 17 classified as having mild, 4 moderate, and 5 severe dizziness-related handicap. A significant correlation was observed between GPE and DHI scores (adjusted $R^2 = 0.446$), and to a lesser extent with vestibulo-ocular reflex (VOR) gain (adjusted $R^2 = 0.272$). Neither age nor gender demonstrated a significant association with overall DHI scores, although there was a non-significant trend toward lower scores in males. Subscale analyses revealed a modest correlation between female gender and higher emotional DHI subscores, as well as between increasing age and higher functional subscores ($p < 0.05$).

Conclusions:

GPE following rapid head movements is a significant predictor of subacute symptom severity in AUVP, accounting for nearly half of the variance in DHI scores. Emotional symptomatology appeared to be more pronounced in females, while functional impairment demonstrated a minor age-related effect.

S14 L11

Vaccine Hesitancy as a Risk Factor for Otologic Dysfunction Following SARS-CoV-2 Infection

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Background:

Beyond its well-documented respiratory effects, SARS-CoV-2 has been associated with a range of additional health complications including those affecting the audiovestibular systems. Some studies have reported instances of sudden hearing loss, vertigo, and other auditory issues in patients post-COVID-19, suggesting a potential link between the virus and inner ear pathology.

Materials and Methods:

This single institution retrospective study of 1,499 COVID-19 positive participants describes the otologic side effects and severity following SARS-CoV-2 infection, compares rates of post-infection otologic symptoms between vaccinated (VP) and unvaccinated participants (UVP), and compares rates of symptoms by vaccine type.

Results:

20% of participants reported dizziness, 10% reported hearing loss, 18% reported aural fullness, 16% reported tinnitus, and 9% reported experiencing otalgia. Unvaccinated patients experienced significantly higher rates of various otologic symptoms associated with COVID-19 infection than vaccinated patients regardless of vaccine type (Pfizer, J&J, Moderna).

Conclusions:

In this current anti-vaccination climate, individuals should be better informed of this protective effect to reduce their risk of hearing loss, aural fullness, tinnitus, and otalgia when deciding whether to receive the COVID-19 vaccine and furthermore, these results may have implications on public health policy.

S15 L1

Understanding Bilateral Vestibulopathy: Insights from the Video Head Impulse Test

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Background: Bilateral vestibulopathy (BV) is a known cause of chronic vestibular syndrome. With the video head impulse test (VHIT), we can now evaluate all six semicircular canals independently, and establish BV subgroups based on canal gain patterns. The objectives were to assess gain patterns for BV, and evaluate subgroups with regards to sex, age and hearing loss.

Materials and Methods: Retrospective chart review was performed of all patients who underwent VHIT between Jan/2021 and July/2024. Patients with lateral canal gains less than 0.7, bilaterally, were included. Results of canal gains, VHIT patterns, audiometry and videonystagmography (VNG) results were reviewed.

Results: 101 cases were included. Patients were 75.5 ± 13.1 years old and 64.4% were women. Various VHIT patterns were observed; the most frequent being decreased canal gains across all six canals (44.6%), followed by a mix of canals with decreased gains with no clear pattern (34.7%). Decreased gains limited to the lateral canals were rare. We did not observe any significant difference between subgroups with regards to gender or age. Concomitant hearing loss was common (89.6%). A trend was noted, suggesting that severity of hearing loss increased with the number of affected canals. An abnormal VNG test was common (73.3%).

Conclusion: Various patterns of canal gains were observed for patients with BV. Audiometry and VNG should be considered as part of BV studies since abnormalities are commonly found. Further research is needed to understand VHIT patterns in BV.

S15 L3

Prognosis of asymptomatic endolymphatic hydrops in healthy volunteers: A five-year cohort study

Tadashi KITAHARA, Takahiro KIMURA, Hiroshi INUI

Backgrounds: This study aimed to clarify the prognosis of asymptomatic endolymphatic hydrops (EH) in healthy volunteers via five-year follow-ups with inner ear magnetic resonance imaging (MRI).

Methods: Inner ear MRI was performed on 115 participants recruited as controls in a previous study on Meniere's disease. The endolymphatic space was visualized using Naganawa's method of contrast-enhanced MRI with intravenous gadolinium injection and evaluated using Nakashima's method of 2D imaging analysis.

Results: Cochlear or vestibular EH was present in 7.0% of participants (n = 8), with all cases being unilateral (laterality), moderate (severity), and asymptomatic (onset). Only cochlear-localized EH, only vestibular-localized EH, and both EH were present in 1.7% (n = 2) (C group), 4.3% (n = 5) (V group), and 0.9% (n = 1) (CV group) of participants, respectively. Conducting inner ear MRI after five years showed that EH had almost disappeared in two participants in the C and V groups (4/8, 50.0%). EH was still present in three participants in the V group and one in the CV group (4/8, 50.0%). One participant in the V group and another in the CV group presented with residual inner ear EH and developed typical symptomatic Meniere's disease (2/8, 25.0%).

Conclusions: Approximately 7% of healthy participants showed asymptomatic EH. Therefore, EH is not the definitive marker for making a diagnosis as Meniere's disease or the suitable predictor for development of Meniere's disease. Among these participants, 25% maintained EH and subsequently developed typical Meniere's disease within the next five years. Schellong-positive participants maintained persistent EH in the inner ear, and participants with higher scores on the self-rating depression scale developed Meniere's symptoms after five years.

S15 L4

Double-blind placebo-controlled crossover study of the effect of prolonged noisy galvanic vestibular stimulation on posture in vestibulopathy

Shinichi Iwasaki, Chisato Fujimoto

Background: A portion of patients with vestibulopathy are refractory to rehabilitation and difficult to treat. This study aimed to evaluate whether long-term noisy galvanic vestibular stimulation (nGVS) improves body balance in patients with vestibulopathy and severe balance impairment.

Methods: A multicentre, randomised, double-blind, placebo-controlled, crossover trial was conducted. Subjects were 20- to 85-year-old patients with vestibulopathy who had been unstable for more than one year and whose symptoms had persisted despite vestibular rehabilitation therapy for more than six months. They were randomly assigned to one of two groups; one group received nGVS first and then the placebo 14 days later, the other group were evaluated in reverse order. The primary outcome was the difference of the mean percent change from the baseline in the velocity of centre of pressure (COP) during 3 h of stimulation between the nGVS and placebo periods, and it was analysed with the mixed effects model.

Results: Twenty and 22 subjects were assigned to the two groups in the full analysis set (FAS). The mean percent change in the velocity of COP during stimulation for 3 h was -9.4 % for nGVS and -12.5 % for placebo. There were no significant effects of nGVS on the velocity in the least-squares means of the difference between nGVS and placebo (3.1 %, p = 0.066).

Conclusion: Long-term nGVS did not ameliorate body balance compared to placebo stimulation in patients with vestibulopathy.

S15 L5

Partial ossicular reconstruction with a novel balljoint prosthesis

Dirk Beutner[1], Thomas Effertz[1], Nicolas Bevis[1]
[1] University of Göttingen

Background:

Middle ear surgery involves reconstruction of the ossicular chain, predominately using rigid implants. New middle ear prostheses strive to mimic the physiologic micromovements of the ossicular chain and prevent dislocation, protrusion, and preloading of the annular ligament due to pressure fluctuations.

Materials and Methods:

In collaboration with MED-EL, we developed a new passive middle ear prosthesis that features a balanced, centered ball joint between the headplate and shaft of the prosthesis. We compared the sound transmission properties of this new prosthesis with those of a standard rigid prosthesis. Using Laser-Doppler-Vibrometry (LDV), we measured the sound-induced velocity of the stapes footplate relative to a given acoustic stimulus.

Results:

The new prosthesis showed equivalent sound transmission characteristics compared to the rigid prosthesis, while retaining the ability to compensate for pressure fluctuations due to its ball joint. This ensures good transmission properties even during displacements of the tympanic membrane. Implantation of the prosthesis in clinical studies proves to be safe and reliable. Clinical data show satisfactory audiological results and demonstrate the effectiveness of the new middle ear prosthesis.

Conclusion:

This development is a further step towards a physiological reconstruction of the ossicular chain.

S15 L6

Inner ear Schwannomas: Preservation of vestibular function and hearing rehabilitation with cochlear implants after surgical tumour removal – our experience in a monocentric case series of 133 patients

Stefan Plontke[1], Gerrit Götze[1], Jonas Scheffler[1], Anna Kopsch[1], Luise Wagner[1], Torsten Rahne[1]

[1] Martin Luther University Halle-Wittenberg

Background: Over the last two decades, interest in the diagnosis and treatment of inner ear schwannomas (IES) including hearing rehabilitation with cochlear implants (CI) has increased (1, 2, 3).

Materials and Methods: Based on a monocentric case series of 133 consecutive patients with inner ear schwannomas, we report the results regarding preservation of vestibular receptor function (measured by vHIT, o/cVEMPs, and calorics) and hearing outcomes with CI after surgical tumour removal with a focus on intracochlear IES. Preoperative and postoperative distributions were compared with paired t-tests.

Results: Here we show that in the case of exclusively intracochlear tumours, there was no significant difference between pre- and post-operative measures for all tests of the five vestibular organs after partial, subtotal, or total cochlectomy. The average monosyllable word recognition score with CI at 65 dB in quite in these patients was more than 10% above the benchmark of the German CI registry.

Conclusions:

In accordance with the results of a recent meta-analysis (1), hearing loss in IES patients can be successfully rehabilitated with CI in most cases regardless of tumour classification. In solely intracochlear IES, the hearing results with CI are above average and the vestibular receptors continue to function independently. These observations have important implications for our understanding of the function and the surgery of the peripheral auditory and vestibular system.

(1) Iannacone FP et al. 2024. doi:10.1007/s00405-024-08818-3

(2) Plontke SK et al. 2025. doi: 10.1097/MAO.0000000000004363

(3) Marinelli JP et al. 2025. doi: 10.1097/MAO.0000000000004362

S15 L7

Solving for Why? Impact of Early Etiologic Assessment on the Access to Bilateral Cochlear Implantation in Children with Hearing Loss.

Sharon Cushing[1]

[1] Hospital for Sick Children

Introduction: Diagnostic confirmation of sensorineural hearing loss (SNHL) in children typically occurred before etiologic assessment until recently when universal hearing screening was expanded to include dried blood spot (DBS) testing to detect congenital cytomegalovirus (CMV) and common mutations in GJB2/6 and SLC26A. Objective: The study aims to assess the impact of identifying hearing loss etiology in neonates through a universal risk factor screening, on diagnosis and intervention. Methods: All children with SNHL from cCMV or genetic mutations (GJB2/6 and SLC26A), detected through universal newborn DBS testing who received cochlear implant(s) (CI) from 2018-2022 were included (n=34). A control group included 34 children receiving CI born with pre-lingual SNHL in 2016, prior to implementation of expanded risk factors screening. Age at diagnostic ABR, hearing aid fitting, MRI and CI were analyzed. Results: In the case group, 21/34 (62%) had SNHL due to genetic mutations with GJB2 being most common (17/21, 81%) and the remainder (13/34, 38%) were diagnosed with cCMV. MRI occurred at a mean of 8 months (SD=6.9) in the case cohort while the control group received MRI at significantly older ages (mean = 32 months, SD = 14), ($P<0.001$). CI occurred at a mean of 13 months (SD = 7.2) in the case group and at significantly older ages in controls (mean=39 months, SD=11.5), ($P<0.001$).Conclusion: Knowing the etiology for SNHL within the first few weeks of life appears to accelerate diagnosis, evaluation and intervention, particularly early bilateral CI.

S15 L8

Sialyllactose preserves residual hearing after cochlear implantation

JEONGHUN JANG, Yun-Hoon Choung

Background: In individuals with hearing loss, protection of residual hearing is essential following cochlear implantation to facilitate acoustic and electric hearing. Hearing preservation requires delivery of the optimal quantity of a pharmacological agent using osmotic pumps. Several studies have reported variable hearing outcomes with osmotic pump-mediated steroid delivery. Several new drugs, including sialyllactose (SL), can prevent tissue overgrowth. This study aimed to identify SL as a new candidate drug and evaluate the prevention effect on hearing loss by cochlear implantation.

Materials and Methods: In the present study, we used an animal model to simulate the damage due to electrode insertion during cochlear implantation. The positive effects of the pharmacological agent SL against insults were evaluated in vitro using HEI-OC1 cells. SL was delivered using osmotic pumps to prevent loss of the residual hearing in this animal model. We demonstrated hearing deterioration and tissue fibrosis and ossification in this model.

Results: Increased gene expressions of inflammatory cytokines were identified in the cochleae following dummy electrode insertion. Following the administration of SL, insertion led to a decrease in hearing threshold shifts, tissue reactions, and inflammatory markers.

Conclusion: These results emphasize the possible role of SL in hearing preservation and improve our understanding of the mechanism underlying hearing loss after cochlear implantation.

S15 L9

CRISPR Exon Skipping for Pendred Syndrome (DFNB4) Hearing Loss: Vestibular Function Restored but Hearing Loss Persists in a Mouse Model

Yen-Fu Cheng, Chen-Chi Wu

CRISPR/Cas9 Exon Skipping Restores Vestibular but Not Auditory Function in DFNB4 Mouse Model

Background:DFNB4-related hearing loss arises from mutations in the SLC26A4 gene, affecting pendrin protein expression and inner ear homeostasis. This study aimed to investigate CRISPR/Cas9-mediated approach as a therapeutic strategy to restore pendrin expression and auditory-vestibular function in DFNB4 hearing loss.

Materials and Methods:Using a DFNB4 mouse model harboring the common Asian SLC26A4 splice-site mutation (c.919-2A>G), we employed CRISPR/Cas9 to remove exons 8 and 9, reframing the transcript for functional pendrin expression. Vestibular function was assessed through locomotor tests. Auditory function was evaluated by auditory brainstem response (ABR), and cochlear histopathology was examined for structural changes.

Results:CRISPR-mediated exon skipping successfully restored pendrin expression in the inner ear and significantly improved vestibular function, eliminating circling behaviors observed in untreated mutant mice. Despite molecular correction, profound hearing loss persisted, evidenced by consistently elevated ABR thresholds and significant cochlear hair cell loss. Cochlear histology showed persistent structural abnormalities, including endolymphatic hydrops.

Conclusion:Exon skipping via CRISPR/Cas9 effectively restored vestibular function and pendrin expression but did not improve auditory outcomes due to irreversible cochlear damage. These findings underscore the therapeutic potential and limitations of gene editing for hereditary inner ear disorders, suggesting that achieving complete auditory rehabilitation may require complementary or earlier interventions.

S16 L1

Metabolization of odorants by human nasal mucosa – a crucial step in olfaction

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Background Human nasal xenobiotic metabolizing enzymes (XMEs) both protect us from inhalable toxicants and interestingly play a crucial role in olfactory peri-receptor events, which are a key step in olfaction. They are known to be present in olfactory mucosa. Since a major part of the nasal cavity is lined by respiratory mucosa, we hypothesize that this tissue also contributes to odorant metabolism.

Material and Methods Primary human nasal epithelial cells and fibroblasts were isolated from surgical specimens of normosmic patients, and tissue models were cultivated using a biological scaffold. Single-cell RNA sequencing and RTqPCR were performed to study XME expression. Furthermore, we confirmed protein abundance by immunohistochemistry and Western blot. To assess XME metabolic activity, tissue models were treated with defined odorants, and metabolites were analyzed by gas chromatography–mass spectrometry.

Results We identified >60 phase I and phase II XME genes in the tissue. From this panel, we selected the phase I XMEs dicarbonyl and L-xylulose reductase, aldehyde dehydrogenase 1A1 and 3A1 for further analyses and verified their protein abundance in nasal tissue models. Our data indicate that the models are capable of metabolizing substrates of these enzyme families, for instance, 3,4-hexanedione to 4-hydroxy-3-hexanone and benzaldehyde to benzyl alcohol and benzoic acid.

Conclusion Human nasal tissue models appear to contribute significantly to odorant metabolism since they express several functional XMEs. This is supported by metabolic activity towards representative aroma compounds occurring in food. We will apply our findings to illuminate different parosmic conditions.

S16 L2

Standardized Endoscopic Optic Nerve Decompression: A Comprehensive Radiological and Anatomical Study

Andrzej Sieskiewicz[1], Tomasz Lyson[2], Zenon Mariak[2], Merek Rogowski[1], Bogdan Ciszek[3]

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Background: Despite expanding indications for endoscopic optic nerve decompression (EOND), standardized guidelines for the optimal extent of decompression remain lacking. This contributes to variability in surgical practice and limits comparability of outcomes. This study proposes a standardized, radiologically guided method for planning EOND, using the lateral optico-carotid recess (LOCR) as a consistent anatomical landmark.

Methods: The extent of endoscopic transnasal decompression was planned using non-standard oblique CT reconstruction planes, parallel and perpendicular to the optic canal, in 60 orbits. Measured parameters included the distance from the orbital apex to the intracranial end of the optic canal and to the point where the optic nerve is enclosed by bone over only 180° of its circumference—defined as the posterior decompression endpoint (PDE). The location of the LOCR was identified relative to these landmarks. EOND was performed in accordance with these measurements, and adequacy of decompression was confirmed via transcranial approach.

Results: The safe endpoint for optic nerve decompression was consistently located within 2.5 mm anterior and 1.3 mm posterior to the medial edge of the LOCR. When measured from the orbital apex, this point ranged from 4.8 to 14.4 mm. All anatomical dissections confirmed complete and accurate decompression based on these measurements.

Conclusions: Non-standard oblique CT reconstructions allow for individualized and precise planning of EOND. This method provides a practical means of standardizing the extent of endoscopic decompression. The LOCR serves as a reliable intraoperative and radiological landmark facilitating optimal decompression of the optic nerve in endoscopic procedures.

S16 L3

Radical Endonasal Surgery Combined with Liposomal Amphotericin B for the Treatment of rhino-orbito-cerebral mucormycosis (ROCM): The MICCA Protocol

Romain KANIA, Fanny LANTERNIER, Benjamin VERILLAUD, Philippe HERMAN, Olivier LORTHOLARY

Background: Rhino-orbito-cerebral mucormycosis (ROCM) is a severe fungal infection, predominantly affecting immunocompromised or diabetic patients, with high mortality rates. Mortality rates range from 20 to 50% and exceed 80% when cerebral involvement is present. Conventional medical and surgical management is often inadequate in controlling the infection. We designed the MICCA Protocol to determine if the combination of radical surgery and liposomal amphotericin B improves local disease control and survival compared to conventional management.

Materials and Methods: The MICCA protocol investigated the effect of radical endonasal surgery, extending to the skull base, combined with liposomal amphotericin B treatment. The primary objective was to evaluate its impact on the 3-month survival rate. This study involved precise radiological staging using CT and MRI at baseline, followed by a radical surgical resection and antifungal therapy. A second-look surgical evaluation and radiological assessment occurred at day 7.

Results: Nine patients (78% male, average age 60) were included. Despite antifungal treatment, the mortality rate was 55.6%. Neurological complications and tissue necrosis were linked to poor outcomes. The disease progressed rapidly, especially in patients with comorbidities like ketoacidosis and anaplasia.

Conclusion: Early surgical revision and close monitoring may improve outcomes. Despite aggressive treatment, mortality remains high, especially in patients with neurological involvement or comorbidities. These findings highlight the importance of earlier diagnosis, control of comorbidities and the need for more effective therapeutic strategies in managing ROCM.

S16 L4

What's good enough in septoplasty?

Ola Sunnergren

Background

Due to lack of evidence, the value of septoplasty has been debated by both rhinologists and health care funders. It is therefore reassuring that two RCTs have shown that septoplasty is more effective than non-surgical treatment of nasal obstruction. Although septoplasty outperforms medical treatment, the question remains whether patients find the surgical results satisfactory. The aim of this study was to compare postoperative NOSE scores with the PROMs "are you satisfied with the result of your septoplasty" and "have your nasal breathing improved after your septoplasty".

Material & Methods

533 adult septoplasty patients who responded to the 12-month PROM questionnaire in the Swedish Quality Register for Septoplasty (SQRS) were included. The response rate was 54.3%, the mean age was 38 years, and 71% were men.

Results

The mean and median NOSE-scores after septoplasty was 30.9 and 25, respectively. Among patients with NOSE-scores better than (i.e. below) the mean, 86% reported both improved nasal breathing and satisfaction with the surgery. Among patients with NOSE scores over the mean, the corresponding rate was 17%.

Conclusion

The mean post-operative NOSE score in the SQRS, 30.9, is in accordance with previous reports from RCTs on septoplasty results. SQRS data, however, indicate that patients do not consider postoperative NOSE-scores over 30 as good enough, as only a small fraction (17%) of these patients reports both satisfaction with the surgery and improved nasal breathing. SQRS data thus indicate that the results presented so far in the scientific literature might not meet many septoplasty patients' expectations.

S17 L1

Meniere's disease: different mechanisms for hydrops and implication of treatments – an update.

Måns Mgnusson[1], Eva Degerman[2], Ann-Ki Pålbrink[2], Rene in t'Zandt in t'Zandt[2]

[1] Copenhagen Hearing and Balance Center, Rigshospitalet, Copenhagen, denmark., [2] Det of Otorhinolaryngology, Lund University Lund Sweden

Background:

The course and symptoms in Meniere's disease vary. While some patients have a high frequency of attacks and continuous symptoms, other have sporadic attacks and several go into remissions that lasts for years. The responses to different treatments are similar. While one patient may respond to a certain treatment, this may not help another. This holds true for most non-destructive approaches. Actually, the literature report that most treatments seems to have a success rate of about 2/3rd. which, resembles the number going into spontaneous remission when observed for several months. We can thus suggest the "two-third problem" in Meniere's disease. The heterogenicity of treatment responses, the number of different treatments suggested and the variety in the spontaneous course and in symptoms, may lead to a suspicion that there is either more than one etiology causing similar symptoms and/or that this is actually more than one disorder.

Meniere's disease is suggested to be related to endolymphatic hydrops, and it is now possible to visualize the endolymphatic compartment with MRI after administration of gadolinium.

Material and Methods:

We have developed an experimental model creating a hydrops in mice, visualizing it with a 9,4T animal MRI system with specially developed sequences Even on a cellular level there seem to be different mechanisms causing hydrops. With implication for treatments.

Results and Conclusion:

We present an overview on treatments relative etiology of Meniere´s disease or hydropic inner ear disease, as based on present knowledge. New data seems to suggest a multi modal therapeutic approach.

S17 L2

Novel dual-lumen microneedle delivers adeno-associated viral vectors in the guinea pig inner ear via the round window membrane

Anil Lalwani[1], Daniella Hammer[1], François Voruz[2], Aykut Aksit[3], Eugénie Breil[1], Francis Rousset[2], Pascal Senn[2], Sten Ilmjärv[4], Elizabeth Olson[1], Jeffrey Kysar[1]

[1] Columbia University Vagelos College of Physicians, [2] University of Geneva, [3] Haystack Medical, [4] Antion Biosciences SA

Background:The clinical need for minimally invasive inner ear diagnostics and therapeutics has grown rapidly, particularly with the development of gene therapies for treating hearing and balance disorders. These therapies often require delivery of large injectate volumes that can cause hearing damage.

Materials and Methods: In response to this challenge, dual-lumen microneedles, with two separate fluidic pathways controlled independently by micropumps, were designed for simultaneous aspiration and delivery to the inner ear across round window membrane(RWM) and were fabricated using 2-photon polymerization(2PP). To assess the proof of concept of the dual-lumen microneedle device, simultaneous injection of 5 µL of adeno-associated virus (AAV) expressing green fluorescent protein (GFP) and aspiration of 5 µL of perilymph was performed in guinea pigs in vivo. Hearing thresholds were measured using auditory brainstem response (ABR) at time points before and 1 week after the procedure. Confocal imaging of the cochlea, utricle, and contralateral inner ear was employed to quantify and characterize the spatial distribution of hair cells with AAV transduction.

Results: Dual-lumen microneedle devices were found to be functional in the surgical setting. There was hearing loss limited to higher frequencies of 24 kHz and 28 kHz with ABR mean threshold shifts of 13 dB sound pressure level (SPL) ($p=0.03$) and 23 dB SPL ($p<0.01$), respectively. Furthermore, cochlear AAV transduction with a stereotypical basoapical gradient was observed in all animals (n=5).

Conclusion: Dual-lumen microneedles can facilitate delivery of large volumes of therapeutic material into the inner ear, overcoming the limitations of single-lumen microneedles.

S17 L3

Linking oxidative stress and inflammation in hearing loss: A journey from the cochlea to the brain

ANNA R. FETONI, FABIOLA PACIELLO, ANNA PISANI, VERONICA MOHAMED, CLAUDIO GRASSI, GAETANO PALUDETTI

The interplay between oxidative stress and inflammation is increasingly recognized as a key pathogenic mechanism in various models of sensorineural hearing loss (SNHL) induced by exogenous factors, including noise exposure and ototoxic drugs. In the central nervous system (CNS), glial cells, particularly microglia and astrocytes, are known to mediate the connection between oxidative imbalance and inflammatory processes. However, their contribution to sensory damage, particularly within the auditory system, remains poorly understood.

In this study, we explored the involvement of oxidative and inflammatory pathways in driving functional, morphological, and molecular alterations in both peripheral (cochlea) and central (auditory cortex, ACx) auditory structures using animal models of hearing loss induced by noise exposure or ototoxic agents. We performed a comprehensive set of analyses, including electrophysiological assessments, histological and immunofluorescence examinations, and molecular profiling of oxidative and inflammatory markers.

Our findings reveal that different models of hearing loss converge on shared pathophysiological mechanisms, characterized by pronounced redox imbalance and inflammatory markers activation in both the cochlea and ACx. This was accompanied by astrocyte and macrophage/microglia activation, upregulation of chemokine receptors, and evidence of inflammasome activation, indicating a robust inflammatory response.

These results underscore the dual role of oxidative stress and inflammation in the progression of auditory dysfunction and suggest that glial cells are pivotal mediators in this process. Targeting these molecular pathways may offer novel therapeutic strategies to mitigate SNHL induced by exogenous factors and preserve auditory function.

S17 L4

Genetics of deafness: Implications for precision medicine

Karen Avraham[1]

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Background: The rapid advancements in high-throughput sequencing have facilitated the identification of pathogenic variants and the discovery of novel genes, bringing in the era of precision medicine. Hearing loss has benefited from this approach due to its genetic and phenotypic heterogeneity, with over 200 deafness-related genes found to date. Nevertheless, up to half of inherited deafness cases remain unsolved. As gene therapy becomes a reality for deafness, it is critical to identify pathogenic variants in each population to implement therapy as it become available for each gene.

Materials and Methods: We analyzed electronic medical records (EMRs) from the Maccabi HMO Biobank to identify hearing impaired individuals, obtained DNA and performed whole-exome sequencing using an Illumina platform. To analyze novel variants, we developed PredHL, a machine-learning model that predicts the impact of pathogenic variants at the protein level by capturing energetic and physico-chemical changes caused by disease mutations. Functional analysis using cell culture and immunolocalization is being used to study a subset of variants. Finally, gene therapy is being implemented on mouse models of human deafness.

Results: We identified 136 variants in 57 genes associated with hearing loss. We successfully restored hearing and balance in a CLIC5 mouse model for deafness.

Conclusion: Our study aims to create a comprehensive map of coding genes associated with deafness and translate select genes into gene therapies with potential for precision medicine. Ultimately, these efforts will enhance patient management and rehabilitation.

S17 L5

Perilymphatic Sampling transcriptomics informs the biology of high electrode impedance after cochlear implantation

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[1] University of Melbourne, [2] Royal Victorian Eye and Ear Hospital, [3] AGRF

Background: Perilymph is readily accessible during cochlear implant surgery and provides a unique opportunity for inner ear diagnostics. Here we report how analysis of micro-RNA (miRNA) can provide unique insights into the biological basis for perioperative objective measures in cochlear implantation.

The objective measure of interest was four-point impedance recorded from the intracochlear electrodes. Four-point impedance rises by >10% the day after surgery in some implant recipients. When this occurs, there is a greater chance that the residual acoustic hearing will be lost. It has been proposed that these impedance changes may reflect florid inflammation.

Aim: To determine whether transcriptomic profiles in perilymph informed the pathologic basis for the impedance changes.

Method: 24 adult cochlear implant recipients underwent perilymphatic sampling prior to cochlear implant insertion. Four-point impedance was measured during surgery, and 1 and 90 days later. A microlitre of perilymph was sampled, subjected to next generation sequencing and n small RNA were aligned to the Homo Sapiens Genome. Differential expression of miRNA was undertaken based upon whether the impedance rose after surgery.

Results: Perilymph sampling did not significantly alter residual acoustic hearing. miRNA associated with acute and chronic inflammatory responses, as well as fibrotic responses, were differentially expressed. Targeted pathway analysis revealed that miRNA associated with fibroblast growth correlated significantly with the rise in four-point impedance one day after implantation ($r=0.8$, $p=0.03$).

Discussion: Transcriptomic analysis supported the interpretation that a rise in four-point impedance the day after cochlear implant surgery is associated with inflammatory and profibrotic processes.

S17 L6

Update on cartilage tissue engineering in otorhinolaryngology

Introduction

The current gold standard of cartilage reconstruction entails the carving and assembly of autologous cartilage grafts. These procedure are highly tedious and skill-dependent. Tissue engineering (TE) provides an alternative approach for producing individually tailored cartilage grafts. For translation of this technology into the clinic, immunocompetent animal models are of utmost concern.

Material and Methods

A model of septal cartilage defects in an autologous rabbit model is described in which different variations of TE cartilage based on porcine nasal decellularized cartilage (DNSC) were applied in comparison to native autologous cartilage grafts and in comparison to subcutaneous cartilage grafts. Analyses included biomechanics, immunohistochemistry and MRI.

Results

Good biocompatibility with mild to moderate inflammatory reactions was demonstrated in all experimental groups. Long-term stable and reliable septal reconstruction was achieved in the study groups with or without prior cell seeding with autologous auricular chondrocytes. Due to slightly better biocompatibility and less pronounced septum deviation, the non-seeded DNSC was favored for possible clinical application and further analysed. DNSC augmented with PDFG-BB enhanced the healing process, as demonstrated by reduced inflammation and enhanced cartilage formation after 16 weeks.

Conclusions

Cartilage tissue engineering remains a promising future treatment option in otorhinolaryngology. Although preclinical knowledge obtained by translational studies is increasing steadily, clinical studies remain rare most likely due to the relatively low number of patients who need treatment and the high costs in times of increasing financial restrictions in European Health Care Systems.

S17 L7

Predicting outcomes following cochlear implantation: Assessment of cochlear health

Wiebke Konerding[1,2], Eugen Kludt[2], Peter Baumhoff[1,2], Thomas Lenarz[2]

[1] Dept. of Experimental Otology, Hannover Medical School, [2] Clinics of Otorhinolaryngology, Hannover Medical School

Outcome prediction still represents an unsolved issue in cochlear implantation. While cochlear implants provide remarkable outcomes in speech comprehension in majority of implanted subjects, 30-50% of the variability in outcomes is unresolved. A large variety of factors contribute to these, including peripheral, central nervous, neurocognitive and device-related factors (e.g. Kral et al., 2016, Lancet Neurol).

Spiral ganglion degeneration is a candidate factor for compromised speech perception in cochlear implant (CI) users. However, there are no measures that can identify such degeneration in human CI recipients. Here I will report of two approaches that allow addressing these aspects: (i) Using guinea pigs, we assessed the impact of controlled focal SGN degeneration on electrical responsiveness and derived an electrophysiological marker for the presence, location and size of such lesions (Konerding et al., 2025, J Neurosci). (ii) Using electrically-evoked compound action potentials in human subjects undergoing cochlear implantation under fluoroscopy, we analyzed the response thresholds and related them to the distance from modiolar axis.

In the animal data we could provide a validated measure (the failure index) that was able to identify the presence of microlesions in the spiral ganglion and identify the electrode that was closest to the lesion. In the animal data we report that the slope of the threshold-distance function allows predicting speech performance following cochlear implantation.

Supported by Deutsche Forschungsgemeinschaft (Cluster of Excellence Hearing4All) and MHH+ Foundation.

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Notes

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References: 1. DUPIXENT Summary of Product Characteristics, 2023. **2.** Gandhi NA, Bennet BL, Graham NMH, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. Nat Rev Drug Discov. 2016;15(1):35-50. doi:10.1038/nrd4624. **3.** Schleimer RP. Immunopathogenesis of chronic rhinosinusitis and nasal polyposis. Annu Rev Pathol. 2017;12:331-357. doi:10.1146/annurev-pathol-052016-100401.

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