International Society of Craniofacial Surgery

ISCFS NEWSLETTER

Volume 2 | Number 1

IN THIS ISSUE:

JANUARY 2025

MESSAGE FROM THE EDITOR

"As we step into 2025, I am filled with immense pride and optimism for the future of our field.'

Dear Colleagues and Members of the International Society of Craniofacial Surgery,

As we step into 2025, I am filled with immense pride and optimism for the future of our field. This new year offers us not just the opportunity to reflect on our past achievements, but also to chart ambitious paths forward in innovation, collaboration, and excellence in craniofacial surgery. Together, we have continued to push the boundaries of what is possible, transforming lives and shaping the future of surgical science.

This October, our biennial Congress will take center stage in Shanghai, China, on October 27–30. This event promises to be a landmark gathering, uniting leading minds, seasoned practitioners, and emerging talents from across the globe. The theme for this year's Congress, *Bridging Frontiers: Innovation and Integration in Craniofacial Surgery*, reflects our collective commitment to advancing our field through cutting-edge research, interdisciplinary collaboration, and global engagement.

Shanghai, a city renowned for its vibrant fusion of tradition and modernity, will provide an inspiring backdrop for this premier event. From groundbreaking plenary sessions to hands-on workshops, we will explore the latest advancements in craniofacial surgery, share transformative case studies, and foster the exchange of ideas that drive our specialty forward. I encourage each of you to mark your calendars and begin planning your participation. The biennial Congress is not just a

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platform for knowledge-sharing; it is a celebration of our shared dedication and passion for making a difference in the lives of our patients.

Beyond the Congress, our society's commitment to continuous education and innovation is evident in our quarterly webinar series, which has grown into a vital resource for members worldwide. These webinars serve as a platform to disseminate the latest knowledge, engage in thought-provoking discussions, and spotlight emerging trends in craniofacial surgery. A heartfelt congratulations is in order for the success of our January webinar, which focused on Facial Contouring Surgery—a rapidly evolving and increasingly significant area within our field. The webinar not only highlighted the extraordinary advancements being made in this domain but also underscored the creative and technical prowess of our members, Drs. Swanson, Lo, and Mu, who continue to pioneer new techniques and approaches.

As we look ahead, the remaining webinars in 2025 promise to be equally engaging and enriching. Each session will delve into critical topics, from advances in craniosynostosis management to innovations in 3D surgical planning, ensuring that our members remain at the forefront of scientific and clinical progress. I urge you to take full advantage of these opportunities, not just to learn but to contribute your insights and experiences. Members will now have access to recordings of past webinars in the new Members Area of our website.

Our society thrives because of the dedication and expertise of its members. Your participation—whether as speakers, authors, researchers, or attendees—is the driving force behind our achievements. As we navigate this year, I encourage each of you to think boldly, collaborate widely, and innovate fearlessly. The challenges we face in craniofacial surgery are complex, but together, we have the ingenuity and determination to overcome them. Let us embrace technology, nurture interdisciplinary partnerships, and mentor the next generation of surgeons to ensure that our field continues to flourish.

On behalf of the editorial team, I want to express my gratitude for your unwavering support of the International Society of Craniofacial Surgery and its initiatives. Your contributions to our community—through research, clinical practice, and education—are what make our society a global leader in advancing craniofacial care. I look forward to seeing many of you in Shanghai this October, where we will celebrate the extraordinary strides we have made and envision the future we are building together. Until then, I wish you a year filled with discovery, collaboration, and impactful innovation. Let us make 2025 a landmark year for craniofacial surgery.

JESSE TAYLOR
ISCFS Secretary-Treasurer
UNITED STATES

MESSAGE FROM THE PRESIDENT

Dear friends and colleagues,

With the passage of time, we are delighted to announce that the 21st Congress of the International Society of Craniofacial Surgery will be held in Shanghai, a city of exquisite scenery, in October 2025, a month dedicated to commemorating gratitude. We are honored and proud to host this prestigious event.

Craniofacial surgery has developed over more than 60 years. As an interdisciplinary field that integrates medical aesthetics, neurosurgery, dentistry, and plastic surgery, it has achieved good development in recent years, which would not have been possible without the efforts and dedication of all the colleagues in our society.

I always remember Paul Tessier's quote in the 1st Craniofacial Congress program. ***(Figure 1)*** Nowadays, countless cutting-edge technologies and innovative ideas are born and spread through our newsletter, webinars and masterclasses,

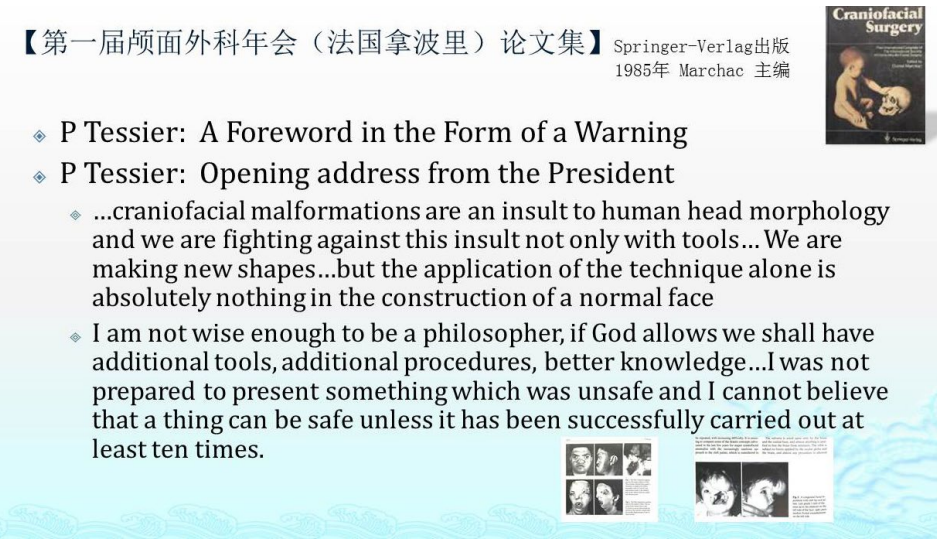

Figure 1

XIONGZHENG MU
ISCFS President
CHINA

"We look forward to meeting again, with a clearer and richer theme, to explore the latest research results, clinical experience and future trends in craniofacial surgery."

injecting strong momentum into the development of craniofacial surgery. Therefore, every academic exchange and discussion is a collision of intellectual sparks in the field of craniofacial surgery, and is an important force driving progress and innovation in the discipline.

We look forward to meeting again, with a clearer and richer theme, to explore the latest research results, clinical experience and future trends in craniofacial surgery. Through a variety of forms such as keynote speeches, thematic discussions, and case sharing, the conference will present the latest progress in craniofacial surgery in an all-round and multi-angle manner, providing a rare opportunity for participants to learn and communicate. We would like to bring in more members and welcome suggestions for modifications to the pre-conference and conference format.

I wish all our colleagues a Happy New Year!

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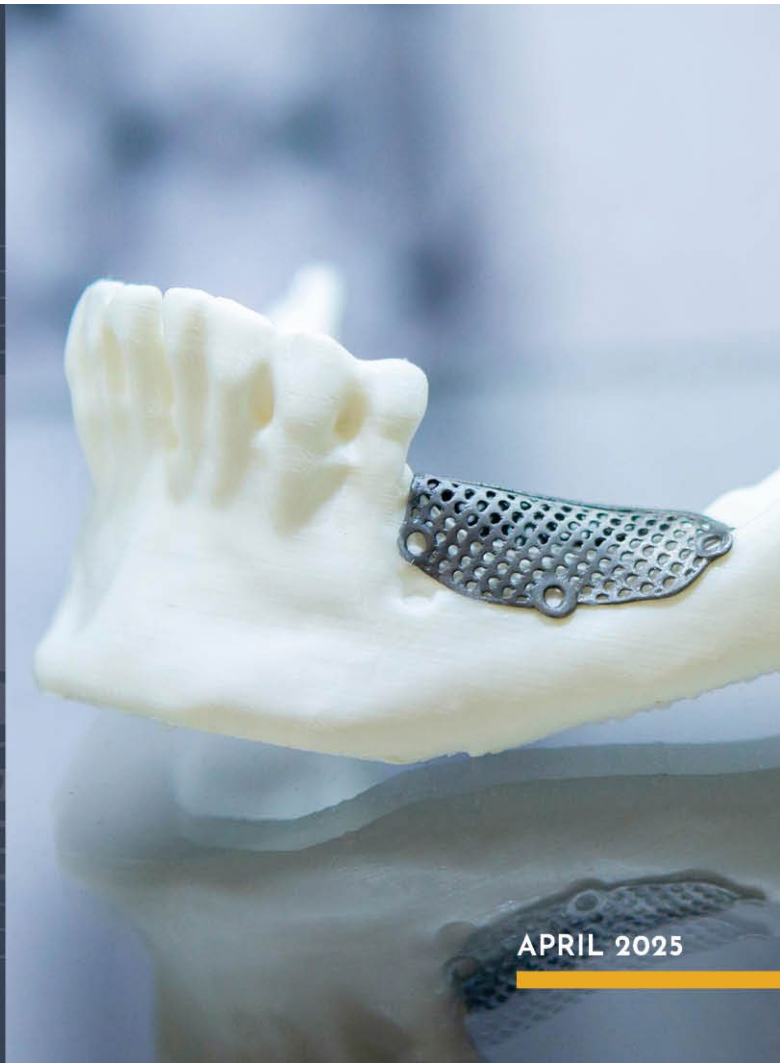
MEMBERS! Please write an article on

HOW I DO IT:

Technique for performing BSSO

To submit an article of 750-1000 words with up to 5 JPG images as needed, send it to admin@iscfs.org no later than Friday, March 14, 2025.



APRIL 2025

21ST ISCFS CONGRESS

SHANGHAI HOTEL

Provided by

VERENA REINMUTH
GERMANY

Secure your booking at the Congress Headquarter Hotel with our exclusive discounts!
Are you ready to elevate your congress experience? Nestled in the heart of Shanghai, the prestigious Shangri-La Jing An offers the perfect blend of luxury, convenience, and state-of-the-art facilities for delegates attending the ISCFS Congress 2025. As our official congress location and headquarters hotel, Shangri-La Jing An promises an unforgettable experience tailored to your needs.

Prime Location for Global Connections
Located in the vibrant Jing An district, Shangri-La Jing An is at the crossroads of business and culture in Shanghai. The hotel boasts direct access to the metro and is a short distance from major attractions, such as the historic Jing An Temple and Nanjing Road - Shanghai's premier shopping destination. This central positioning ensures seamless connectivity for both local and international delegates.

Luxurious Accommodations Tailored for Delegates
Delegates can unwind in the hotel's elegantly designed rooms and suites, each offering panoramic views of the city skyline. Equipped with premium amenities, including plush bedding, spacious work desks, and luxurious bathrooms, the accommodations provide the perfect retreat after a day of networking and learning. Booking your stay at Shangri-La Jing An ensures proximity to all congress activities, eliminating travel hassles and allowing you to make the most of your time. Staying on-site also provides delegates with seamless access to all event venues and maximizes opportunities to connect with peers and industry leaders throughout the congress.

Wellness and Relaxation
Maintaining your well-being is effortless at Shangri-La Jing An. The hotel features a fully equipped fitness center, a heated indoor pool, and CHI, The Spa, where guests can rejuvenate with a range of holistic treatments. These amenities ensure that delegates can stay energized and refreshed throughout their stay.

Your Gateway to Shanghai
Beyond the conference, Shangri-La Jing An offers an ideal base to explore Shanghai's dynamic blend of tradition and modernity. Delegates can discover the city's iconic landmarks, indulge in vibrant nightlife, or immerse themselves in the rich cultural heritage that makes Shanghai a global metropolis.

Let Shangri-La Jing An be the cornerstone of your congress experience. Reserve your spot today and discover why it is the premier choice for discerning delegates from around the globe.

CLICK HERE for more information and the link to reserve your room.

21ST ISCFS CONGRESS

SUBMIT YOUR ABSTRACT!

We welcome readers to submit abstracts for the **21st International Congress of ISCFS in Shanghai, China on October 27-30, 2025**. The submission deadline is **April 30**.

Notification of accepted or rejected abstracts as determined by the Scientific Program Committee will be emailed to submitters on **June 10**.

SUBMISSION LINK:

https://app.oxfordabstracts.com/stages/76197/submitter

ABSTRACT CATEGORIES

- Non-Syndromic Craniosynostosis
- Syndromic Craniosynostosis
- Facial Dysostosis
- Craniofacial Clefts or Encephaloceles
- Craniofacial Feminization Surgery and Facial Contouring Surgery
- Cranio-Maxillofacial Trauma
- Breathing Difficulties and Airway Management
- Maxillofacial and Orthodontic Aspects of Craniofacial Surgery
- Craniofacial Team Coordination and Care Pathways
- Simulation Surgical Education
- Virtual Surgical Planning and Surgical Simulation
- Artificial Intelligence, Augmented Reality, Virtual Reality
- Craniofacial Basic Science
- Neurosurgical Considerations in Craniofacial Surgery
- Distraction Osteogenesis of The Craniofacial Skeleton
- Tumors and Microsurgery in Craniofacial Surgery
- Tumors and Vascular Anomalies
- Cleft and Palate - Complicated or Secondary Problems
- Craniofacial Microsomia including Microtia

SUBMISSION RULES:

1. Abstracts are limited to 350 words with no images or tables.
2. Any number of abstracts may be submitted; however, each Congress participant may present only ONE podium presentation and ONE poster.
3. The official language of the Congress is English, both for submission and podium or poster presentations.
4. Additional accepted abstracts may be assigned to another author or withdrawn.
5. Submitted abstracts that have been presented at national meetings will be considered, but first-time presentations are preferred.

We look forward to reading your abstract(s).

21ST ISCFS CONGRESS

"...one of Shanghai's most prestigious and fashionable business and commercial districts."

Provided by

XIONGZHENG MU

ISCFS President

CHINA

XIANXIAN YANG

CHINA

SHANGHAI FACTS AND HISTORY

SHANGHAI DIALECTS

The prevailing local dialect in Shanghai is the modern Wu – today's southern Jiangsu province – dialect of the Taihu Lake area, which is the inheritance and development of the ancient Wu dialect. Nowadays, the Shanghai dialect varies within five dialect areas in terms of their ancient tones – Chongming, Liantang, Songjiang, Jiabao (Jiading and Baoshan), and the downtown area.

Throughout Shanghai's history, the population and settlements of residents have been quite complicated. In addition to the prevailing Shanghai dialect, other dialects such as the Ningbo, Shaoxing, Suzhou, Wuxi, and northern Jiangsu dialects, as well as Cantonese are still used in Shanghai and have ongoing influence today.

Source: Shanghai Almanac 2023

AREA ATTRACTIONS

Our Congress hotel, Jing An Shangri-La, Shanghai, is located in the Jing An Business District, one of Shanghai's most prestigious and fashionable business and commercial areas.

The hotel sits on a network of public transportation, including Metro Lines 2, 7 and 14. It is about 45-minute drive from Pudong International Airport and only 20 minutes from Hongqiao Airport via the adjacent elevated Yan'an Middle Ring Road.

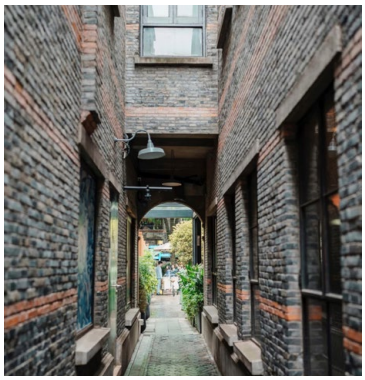
1. **Jing An Temple**: A short walk from the hotel, this is a must-visit for its cultural and historic significance.
2. **Xin Tian Di**: A large-scale, master-planned city-core redevelopment project, consisting of residential, office, retail, entertainment, and cultural properties in the heart of the city. This flagship development integrates early 20th-century Shikumen architecture with contemporary urban lifestyle, fashion elements, modern features, and facilities. It has become a leading lifestyle landmark in the city, offering a rejuvenated Shikumen-style district where visitors

enjoy vibrant culture, entertainment, and food and beverage experiences mixing Shikumen architecture with modern urban fashion style. Awards include being named one of the Top 20 Cultural Landmarks in the World by Forbes and a Classic Case of Urban Renewal in the World by the World Bank.

3. **The Bund**: One of the most iconic and historic places in Shanghai, this famous waterfront region is a symbol of the city's rich history and its rapid development into a modern metropolis.
4. **Yu Garden**: A must-see destination for anyone interested in traditional Chinese architecture, culture, and history. Its unique features, symbolic meaning, and festive atmosphere make it a fascinating and memorable experience for visitors of all ages. The garden serves as a window into China's complex history and cultural traditions, providing a peaceful retreat from the urban hustle of Shanghai.
5. **Jing An Kerry Center**: The hotel is situated within this large-scale integrated complex that includes shopping, offices, and residences. It offers a variety of retail stores and dining options.
6. **Plaza 66**: Known as one of the tallest buildings in Puxi, it houses numerous high-end brands and is a stone's throw from the hotel.

ATTRACTIONS SURROUNDING

JingAn Temple – 5 mins by walk



Xin Tian Di – 10 mins by car

Jing An Kerry Center – located

The Bund – 10 mins by car

Yu Garden – 10 mins by car

Plaza 66 – 5 mins by walk

ISCFS BULLETIN BOARD

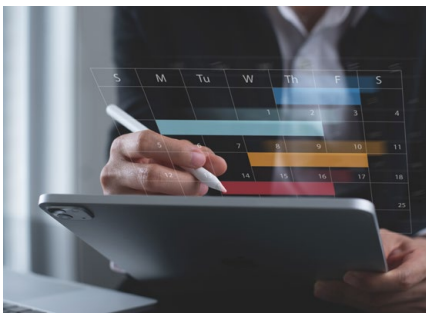
THANK YOU!

To our members who have paid their 2025 annual fee.

Click here if you require an invoice to make a payment.

WEBSITE ADDS MEMBERS' AREA

We are pleased to announce a new feature of the ISCFS website with the addition of a Members' Area. Access is password protected and members are asked to confirm or update their contact information as soon as possible. Some of the contact information will be public facing at the discretion of each member in the form of a Find a Surgeon section on the main site. Previously recorded Webinars will be posted in this area for repeat viewing at any time. An easy to complete application to post Fellowships offered by our members will be included.



New features include:

- ISCFS Video Library
- ISCFS Photo Gallery
- Members Directory
- Link to Renew Membership
- Fellowship Listing Questionnaire

We welcome suggestions from current members concerning the content already included or suggested for future additions to this new area of the website.

Take a look now!

NEW! FELLOWSHIP DIRECTORY

Many of our members offer fellowship programs. As part of our ongoing commitment to provide various educational opportunities, we are initiating a new Fellowship Directory on the website. Members can complete a simple form to include information about fellowships they offer. Those interested in more information about any fellowship listed will be asked to contact the program directly.

The following disclaimer will be included:

The International Society of Craniofacial Surgery (ISCFS) has no influence over or responsibility for the training content or admission of applicants to Fellowships offered by our members. All arrangements regarding program duration, travel, stipends, and housing are entirely between each individual program and the Fellow. ISCFS provides this listing as a service to our members and trainees in the interest of providing ongoing education, training and sharing or skills and ideas.

Log in to the Members' Area and there you will find the Fellowship Submission form under "Member Benefits."

NEXT WEBINAR TOPIC – APRIL

Chiari Malformation – Separating Fact from Fiction

April 15, 2025 | 20:00 pm UTC

Join us on Wednesday, April 15, 2025, at 20:00 pm UTC for an in-depth discussion on "Chiari Malformation – Separating Fact and Fiction" with panelists Drs. Jay Jayamohan (United Kingdom), Giovanna Paternoster (France). Moderator: Jesse Taylor (United States).

TRAVEL TO EUROPE – NEW REQUIREMENTS

Beginning in mid-2025, the rules for visa-free travel to Europe will change for travelers coming from approximately 60 countries and territories. You may be required to get ETIAS travel authorization prior to your departure. It will be a simple on-line form, costing about $7.00, and is required for visitors to many European countries.

To learn more, go to this website: https://travel-europe.europa.eu/etias_en

HOW I DO IT: SPLIT CALVARIAL BONE GRAFTS: HOW YOUNG AND HOW

SPLIT CALVARIAL BONE GRAFTING FOR CRANIOMAXILLOFACIAL RECONSTRUCTION – THE DALLAS TECHNIQUE

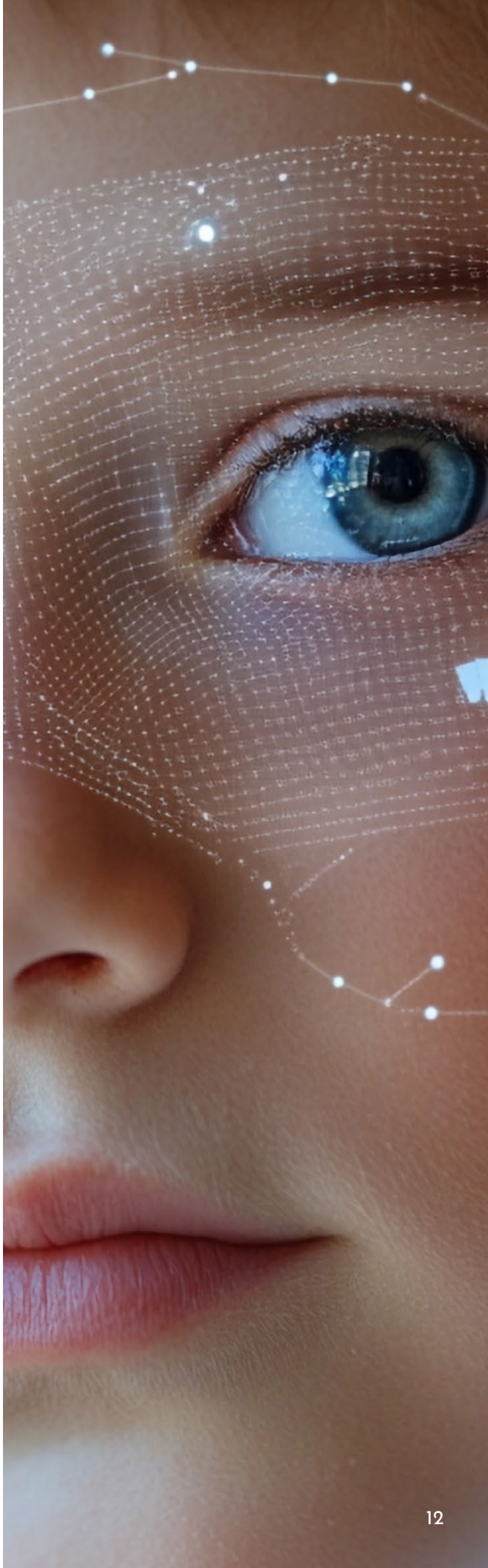
DEMETRIUS M. COOMBS
UNITED STATES

JEFFREY A. FEARON
UNITED STATES

Cranial bone grafts can be harvested by one of two methods: either *in-situ*, when only small grafts are needed, or *ex-situ*, when larger harvest amounts are necessary. For craniofacial surgeons, the most common conditions requiring significant amounts of bone are the secondary repairs of acquired skull defects and reconstructing the bony deficits created by expanding the skull during craniosynostosis corrections. Considering the above, the following description will focus solely on an *ex-situ* cranial bone graft harvest technique.

BASIC CONCEPTS:

- It is possible to split calvarial bone in any age, even including very early in infancy.
- In general, the diploic space



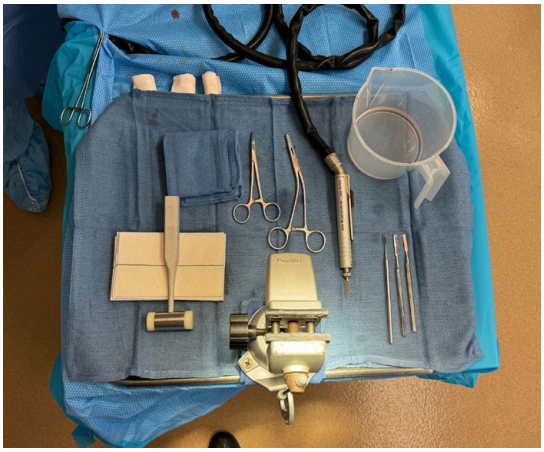


Figure 1

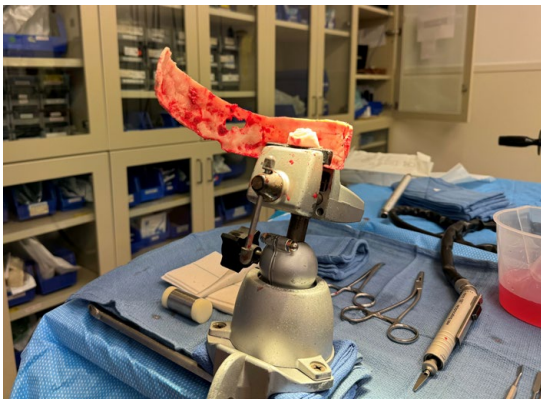


Figure 2

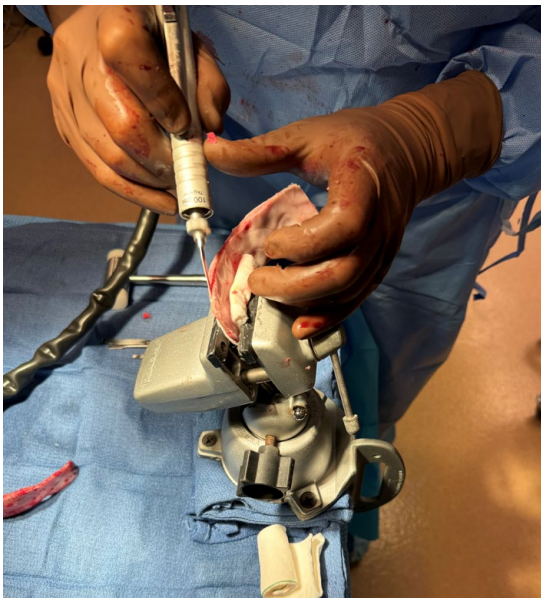


Figure 3

gets thicker towards the vertex, but becomes thinner more inferiorly.
- It is not possible to split bone across a suture.
- Coronal slices on CT scans provide optimal visualization of where the diploic spaces are located and are also helpful in secondary cases for assessing potential harvest amounts.

SURGICAL TECHNIQUE

The key to any successful bone graft harvest is firm stabilization. For this purpose, we prefer to use a sterilized table vise (*Panavise* 301, with 311 bench clamp base), which can be ordered on the Internet. Intraoperative setup includes a sterile back table containing the vise, a pneumatic reciprocating saw (electric saws do not provide sufficient long-term power), a mallet, a curved Kelly hemostat, Tessier bone holding forceps, narrow osteotomes of varying thicknesses, a basin containing antibiotic irrigation (normal saline with gentamycin), multiple large neuro sponge patties, and a dedicated operating room light ***(Figure 1)***.

Once a neurosurgeon has removed the desired bone flap, holding the bone up to a bright light can help to delineate areas of thicker and thinner bone, to better target the splitable regions.

The bone flap is first secured into the vise, with padding on either side, using rolled, moistened, neuro sponge patties ***(Figure 2)***. Padding is arranged to accommodate the curvature of the bone, which avoids an inadvertent fracture when tightening the vise.

In younger infants, the saw is fitted with an extra thin, 25.5 x 0.25mm, blade (ConMed; Utica, NY). This can be used to create a groove along the bony edge ***(Figure 3)***, which helps to facilitate dissection with an extra thin osteotome into the diminutive diploic space. Next, using firm pressure and rocking back-and-forth, the bone should split relatively easily using just the osteotome. This technique can sometimes yield much larger grafts than would have been possible by relying completely on a saw. On occasion, removing the bone from the vise and resting it on the table, can help facilitate a deeper split.

In older children, and adults, more reliance on the saw is necessary due to denser diploic space. Using a vise to hold the bone stable becomes even more important. Once the saw dissection has extended as deeply as possible, the split is finished with an osteotome. However, when faced with a thin, copper-beaten, and irregular inner cortical surface, removing the bone from the vise and holding it with a Tessier bone clamp can permit angling the saw in ways that would

otherwise not be possible in a vise. This technique is best for harvesting bone from the middle of the flap, when the periphery is too thin to split. In certain instances, when encountering areas of excessive bone thickness, multiple grafts may be harvested from the same location, similar to a deli meat slicer, to yield additional grafts from the same section of bone.

Harvested grafts are placed into the basin containing antibiotic irrigation until reconstruction is undertaken. At that time, the grafts are laid onto a clean surgical towel to facilitate efficient selection and placement ***(Figure 4)***. At our center in Dallas, larger grafts are secured with 2-0 PDS (polydioxanone) sutures, while smaller grafts are strategically placed into the tinier defects and covered with Surgicel (Ethicon; Raritan, NJ), which is then dampened with irrigation solution, prior to scalp closure ***(Figure 5)***. By the end of the procedure, the goal should be an intact skull, with no remaining skull defects. If pericranial flaps were dissected upon opening, these are repositioned, before sewing them together over the Surgicel, to further secure the reconstruction.

Neither author has any financial relationship with companies mentioned in this article.

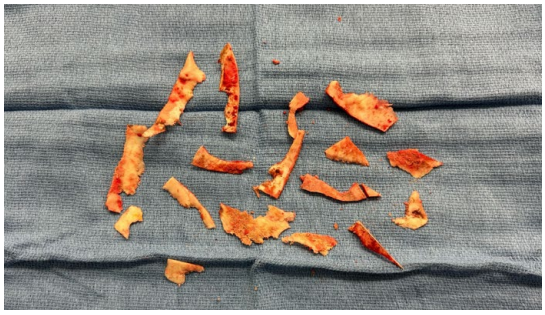


Figure 4

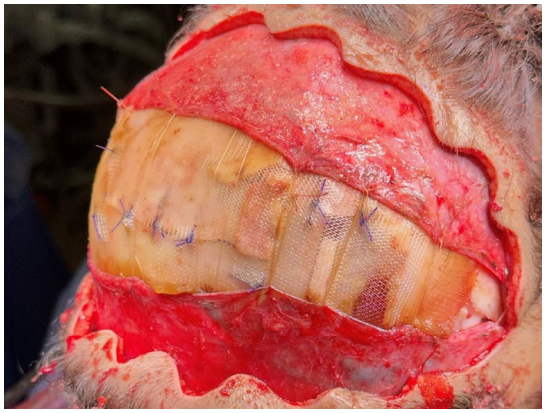


Figure 5

SPLIT CALVARIAL BONE GRAFTS – HOW YOUNG AND HOW

"The Tessier bone bender is very effective in contouring split calvarial bone grafts..'

JORDAN SWANSON
UNITED STATES

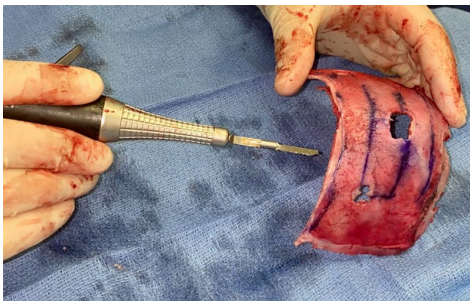


Figure 1

The split calvarial bone graft is arguably the most fundamental procedure of the craniofacial surgeon. It both demands focused technical precision in separating cranial tables through the diploë plane to preserve bone integrity, and is widely applicable for reconstruction of the craniofacial skeleton for craniosynostosis, tumor, and trauma. Split calvarial grafts were conventionally described in children older than 18-24 months when the thickening skull was thought to have sufficient diploë (the spongy trabecular bone that separates the inner and outer layers of the skull's cortical bone). However, technical and technological advancements enable this to be applied to primary cranial vault remodeling procedures.

Many patients aged 8-10 months of age have multiple areas of diploë formation of critical surface area size (2x3cm or greater) to harvest grafts of a useful size. These are often in the parasagittal regions of the skull, and review of a preoperative CT scan can sometimes tip the surgeon off to these locations. A standard reciprocating saw is often thicker than ideal to cut into the diploë of infants under a year of age. However, a micro-reciprocating saw (Aesculap Elan 4 blade GP545R) is 0.3mm thick and 20mm long with a curved tip, and smoothly penetrates thin diploë ***(Figure 1)***. As an alternative, a curved, thin piezoelectric saw can also be used (Mectron MT9-13 osteotomy microsaw, 0.35mm thick.) Because the micro-reciprocating saw is flexible, once introduced parallel to the cortices through the diploë, it tends to follow the curvature of the diploë rather than cutting through the bordering cranial cortices. By hubbing the blade, a 2cm wide graft can be separated. Next, cutting perpendicularly through the inner cortex along the planned margin enables the osteotome to split the cranium precisely ***(Figure 2)***. Often, in patients aged 8-10 months of age, a total of 15-20cm2 of split cortical bone graft can be obtained; less in younger and more in older patients.

The osteogenic effect of dura and pericranium tend to abate with age, conveniently paralleling the emergence of diploë and availability of split cortical bone grafts. Several studies have shown the variability of ossification and persistence of cranial defects when this osteogenic potential, perhaps coupled with bone dust from the craniotome, is relied upon to achieve cranial integrity. In patients who present with craniosynostosis after 3-4 months of age or who are

otherwise not good candidates for suturectomy-based cranial remodeling methods involving cranial springs, distractors, or molding orthoses, I typically perform posterior cranial vault remodeling at 6-9 months and fronto-orbital advancement at 8-10 months of age, and aim to utilize split calvarial grafts in each of these patients.

For the past five years, influenced by Marchac, Fearon, and the Oxford Craniofacial Unit who have utilized single-segment parietal bone grafts for forehead revision or reconstruction, I favor a neo-frontal bandeau reconstruction of the forehead and orbits for most cases of craniosynostosis with anterior dysmorphology. The large fronto-parietal defect and donor site is partially reconstructed by cortical grafts obtained from the dysmorphic frontal bone; however, expansion dictates additional surface area. Split calvarial bone offers dual advantages of increased reliability of ossification and structural integrity of the construct. The Tessier bone bender is very effective in contouring split calvarial bone grafts, and utilizing bone cutting pliers or reciprocating saw to precisely shape the margins to exactly align and fit adjoining bone improves construct stability and contour. Bone grafts are fixated with tightly-tied resorbable PDS sutures (Ethicon), with occasional use of resorbable PGS plates (DePuy Synthes or KLS Martin) ***(Figure 3)***.

Split calvarial bone graft is not a panacea and there can be diminishing returns in patients with thinner calvaria. Cortical bone shavings from a disposable harvesting device (SafeScraper, Geistlich, Switzerland) are a useful adjunct to split calvarial grafts, and can be used in smaller defects or if there is inadequate split cortical bone ***(Figure 4)***. This is harvested from inner cortices of graft segments that are not split, or from external cranial bone away from the reconstruction site. Typically, 20-50cc of cortical graft is harvested and utilized in a cranial vault reconstruction.

Finally, increased facility with split calvarial bone grafts in vault reconstruction of younger patients may also better prepare surgeons to use such grafts in other clinical cases. For example, recently a 15-year-old female with an expansive, heterogenous right frontal bone lesion with cavitation of the outer cortex presented for excisional biopsy of the affected cortical and trabecular lesion, with preservation of the inner cortex ***(Figure 5)***. A split calvarial bone graft, harvested extracranially, enabled simultaneous reconstruction of the outer cortex and diploë ***(Figure 6, prior to placing cortical shavings around the margins)*** with cortical bone shavings similarly placed to the parietal partial-thickness donor site. An adequate contour was achieved (and pathologic examination determined an atypical fibrous dysplasia.)

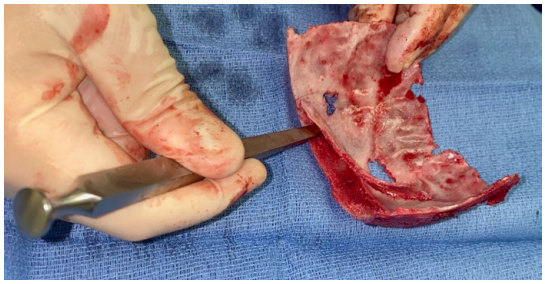


Figure 2

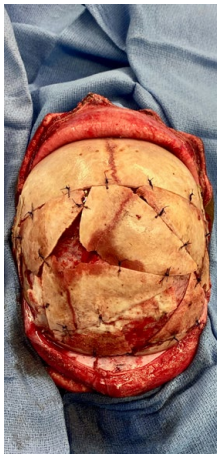


Figure 3

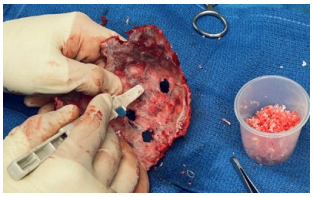


Figure 4

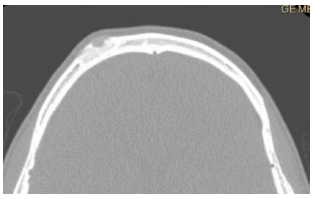


Figure 5

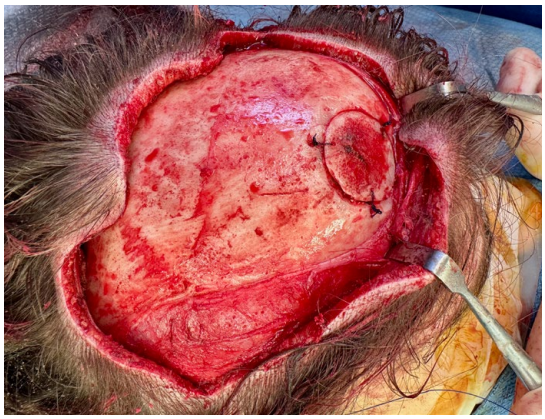


Figure 6

The author has no financial relationship with companies mentioned in this article.

WINDOW INTO HISTORY

ENCEPHALOCELES - THE FIRST SYSTEMATIC REVIEW IN MEDICAL LITERATURE

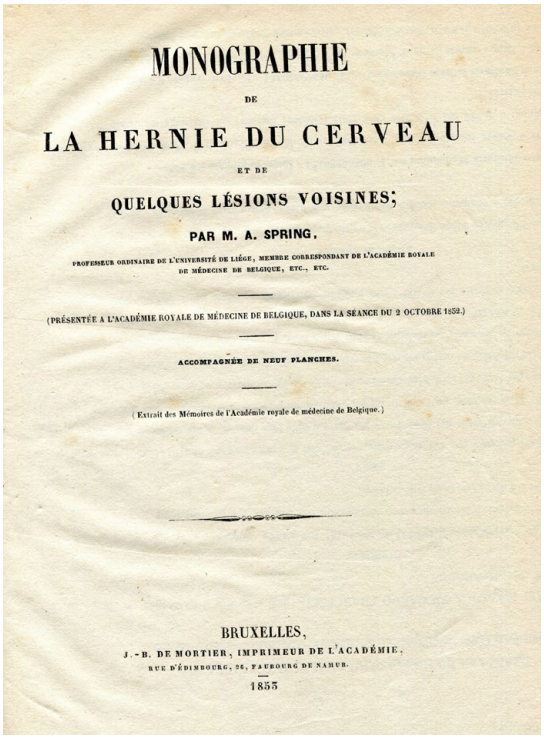
The German anatomist and physiologist **Antoine Frédéric Spring** (1814-1872) was born in Gerolsbach (Bavaria) and studied Botany and Medicine at the University of München. Having obtained a medical degree in 1836, he moved to Liège (Belgium), where he was appointed Professor of Physiology and Anatomy at the University there. During this period, he conducted numerous studies in the fields of human pathology, cholera, and other areas of medical interest. As a botanist, he published an important monograph on Lycopodiaces, a diverse and ancient family of club mosses containing more than 400 species. He died in Liège in 1872.

In 1853, he published the most complete account on encephaloceles ever written. **Monographie de la Hernie du Cerveau et de quelques Lésions voisines** (*Monograph on Brain Hernia and adjacent lesions*) ***(Figure 1)***, is a 198-page work written in French and presented to the Belgian Royal Academy of Medicine on October 2, 1852. It includes the description and illustration of the most typical examples of encephaloceles reported in the literature at the time. To these Spring added some cases of his own. For each of the examined creatures he included a gross description of the site of the herniation, the form of the bulge, the most likely ossification defect, and finally he tried to identify the pathogenesis of the herniation. He was surprised by the frequency with which cerebral hernias occur in the occipital ***(Figure 2)*** and frontal regions, possibly caused by a late ossification defect associated with an increase of intracranial pressure.

Spring proposed a classification of the different types of meningoencephaloceles: simple, when only the brain tissue herniates through the bony gap in the skull, and *complicated* when a collection of serous fluid is associated with brain tissue.

RICCARDO F. MAZZOLA
History Editor
ITALY

"Spring proposed a classification of the different types of meningoencephaloceles..."



MONOGRAPHIE

DE

LA HERNIE DU CERVEAU

ET DE

QUELQUES LÉSIONS VOISINES;

PAR M. A. SPRING.

PROFESSEUR ORDINAIRE DE L'UNIVERSITÉ DE LIÉGE, MEMBRE CORRESPONDANT DE L'ACADÉMIE ROYALE DE MÉDECINE DE BELGIQUE, ETC., ETC.

(PRÉSENTÉE A L'ACADÉMIE ROYALE DE MÉDECINE DE BELGIQUE, DANS LA SEANCE DU 2 OCTOBRE 1852.)

ACCOMPAGNÉE DE NEUF PLANCHES.

(Extrait des Mémoires de l'Académie royale de médecine de Belgique.)

BRUXELLES,

J.-B. DE MORTIER, IMPRIMEUR DE L'ACADÉMIE,

RUE D'ÉDIMBOURG, 26, FAUBOURG DE NAMUR.

1853

Figure 1 - Title page of Monographie de la Hernie du Cerveau et de quelques Lésions voisines (Monograph on Brain Hernias and on some nearby Defects) by Antoine Frédéric Spring

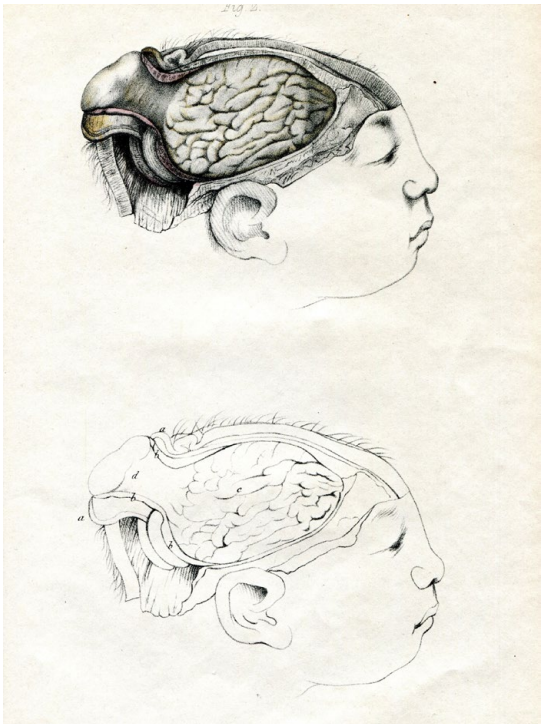
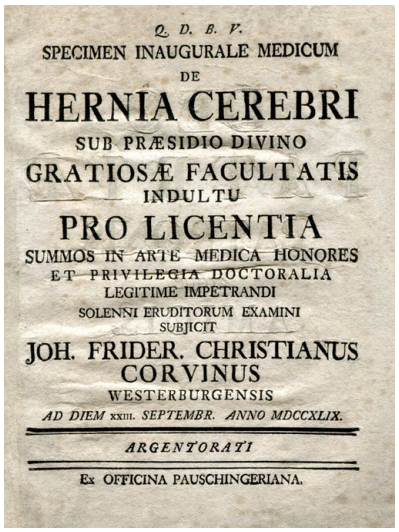


Figure 2 – Newborn with occipital encephaloceles. From: Spring AF. Monographie de la Hernie du Cerveau, 1853

He considered the thesis of the German **Johannes Friedrich Corvinus** (c. 18th Century) presented at Strassburg University in 1749 to graduate in medicine ***(Figure 3)***, [2], as the first scientific account on cerebral hernia. Corvinus stated that cerebral hernias may occur in the frontal, occipital ***(Figure 4)***, or parietal region and coined the term encephaloceles, to indicate this particular clinical situation.



Q. D. B. V.

SPECIMEN INAUGURALE MEDICUM

DE

HERNIA CEREBRI

SUB PRÆSIDIO DIVINO

GRATIOSÆ FACULTATIS

INDULTU

PRO LICENTIA

SUMMOS IN ARTE MEDICA HONORES

ET PRIVILEGIA DOCTORALIA

LEGITIME IMPETRANDI

SOLENNI ERUDITORUM EXAMINI

SUBJICIT

JOH. FRIDER. CHRISTIANUS

CORVINUS

WESTERBURGENSIS

AD DIEM XXIII. SEPTEMBR. ANNO MDCCXLIX.

ARGENTORATI

Ex OFFICINA PAUSCHINGERIANA.

Figure 3 – Title page of Dissertatio de Hernia Cerebri (Thesis on Brain Hernia) by JFC Corvinus, 1749

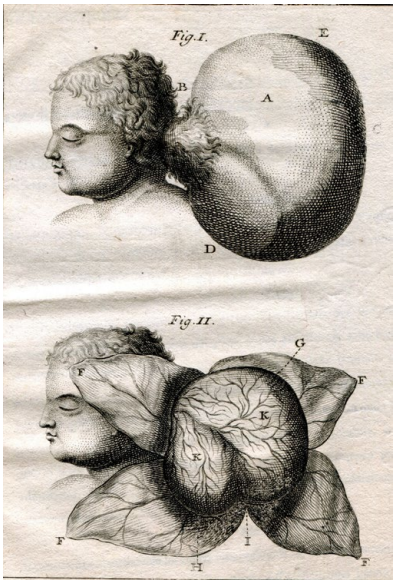


Figure 4 - Newborn with occipital encephaloceles. From: JFC Corvinus. Dissertatio de Hernia Cerebri, 1749

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NEUROSURGERY CORNER

"In patients who are showing agreed worsening of these findings, it will first be important to exclude raised intracranial pressure as a potential contribution. This may require intracranial pressure monitoring."

JAY JAYAMOHAN
Neurosurgery Editor
UNITED KINGDOM

Many patients with craniofacial conditions will also be found to have a condition described as a Chiari malformation. This is normally picked up by a CT or MRI scan. Having cerebellar tonsils more than 5 mm below the foramen magnum will usually be sufficient for a radiological diagnosis. However, I would urge separation between a true malformation and tonsillar herniation. The difference is really in the relationship between intracranial pressure and the development of this anatomical condition.

A true Chiari malformation can develop with normal intracranial pressure and will sometimes require direct surgical treatment if causing symptoms (see below). On the other hand, raised intracranial pressure can cause multiple herniation syndromes throughout the supra and infra territorial spaces, of which cerebellar tonsil herniation is just one. The treatment for herniation is really about treating the cause of the underlying intracranial pressure.

The most important way to distinguish between these two conditions is of course history and examination. So, for example, a patient who has significant early morning headaches, Valsalva or cough impulse headaches, and eye changes such as papilloedema is likely to have raised intracranial pressure. While they may also have a true Chiari malformation, care should be given to try to distinguish between these diagnoses. If they are both present, it would be universal practice that the intracranial pressure would need to be treated before any Chiari malformation. Operating on a foramen magnum in a patient with significantly raised intracranial pressure can be a disastrous procedure with real risk to life for the patient.

A true Chiari malformation may be completely asymptomatic, and these will be seen in a lot of patients with syndromic craniosynostosis. If symptoms are present these can be split into several different categories.

There can be long tract findings in the arms or the legs. Thus, patients may complain of pins and needles or tingling in the limbs, poor coordination in the hands (writing, eating, doing up buttons, typing and playing on phones and consoles), and balance problems when walking. One of the things that many mobile patients complain of is altered

sensation almost as if they're walking on cotton wool. It is rare for patients to have sphincter problems secondary to this condition but not impossible.

The next conglomeration of findings have to do with the functions at the cranio cervical junction with the cranial nerves. Thus, patients may complain of problems with swallowing, in particular of liquids. There may be a history of repetitive chest infections which require further assessment to ensure they are not caused by aspiration. Many patients will notice that their ability to chew and swallow becomes slower and parents in particular will complain that the rest of the family have finished their food and this particular child is still only a quarter of the way through. Take care to look for swallowing problems when there are unconsciously provided provisions such as sippy cups, which families will have continued to use for their children without realising what they were in fact semi-treating.

There can be delays in speech and language development, and of course it is important to look for this when there can be difficulties separating neurological origins from physical changes within the oropharynx which may more easily be picked up and "get the blame."

It is difficult to note for example altered sensation on the face in children, compared to the limbs, but it is worth looking for altered sensation at the back of the throat as part of this assessment.

The other central condition often seen will be eye control. Development of diplopia or palsies of the trochlear and/or abducens nerves may be noted and will require detailed assessment. While it may not be a big enough indication to do surgery directly, progressive palsies may be important to consider as part of an assessment for surgical treatment for a Chiari malformation.

Touching briefly now on treatment options, it would be usual in my unit, and in many European centres, to only treat patients with progressive symptoms and signs. This requires regular careful follow up, ideally with the same team to be able to pick up subtle but definitive progression.

In patients who are showing agreed worsening of these findings, it will first be important to exclude raised intracranial pressure as a potential contribution. This may require intracranial pressure monitoring.

Once this is excluded and if surgical intervention is required, timing for this would usually be considered with the premise that surgery is aimed at stopping things getting worse, rather than necessarily seeing an improvement in the problems already developed. There can therefore be a relatively tight time to perform this procedure.

Although there are of course individual variations, it is often suggested to me by my American colleagues that it is worth offering "prophylactic surgery" in order to keep the long-term symptom burden as minimal as possible. In their view, given the fact that I wait for symptoms to worsen before operating, I am therefore leaving my patients with that progressive set of symptoms long term, which would not have been present had I operated as soon as the diagnosis had been made. Of course, this requires a balance with the risks of surgery which are not insubstantial.

Patients with craniofacial conditions will have super-added risks with abnormal venous drainage and abnormal anatomy of the cranial cervical junction which means that such procedures should only be done by neurosurgeons with sufficient training and skills in this particular condition in this particular patient group.

This is a complex condition in patients with many competing and indeed conflicting conditions. Careful assessment, discussion and planning is needed within an experienced team to provide the best timed and designed treatment – an area we hope to cover in an upcoming discussion online.

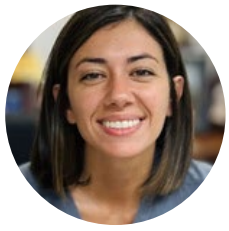
Watch for the April ISCFS Webinar on ***Chiari Malformation: Separating Fact and Fiction***.

Click here to register.

ORTHODONTIC CORNER

"Cleidocranial dysplasia (CCD) is a rare congenital bone disorder with an autosomal dominant pattern of inheritance, with a prevalence of 1 in one million individuals. "

DANIEL LEVY-BERCOWSKI
UNITED STATES



MARIELENA LAYUNO MATOS
PUERTO RICO

CLEIDOCRANIAL DYSPLASIA: A MULTIDISCIPLINARY APPROACH

AIM

This clinical report outlines a multidisciplinary approach for a patient with Cleidocranial Dysplasia (CCD). The patient required surgical exposure of several impacted teeth in the upper arch and preparation for a Le Fort I osteotomy to advance the maxilla. Additionally, this report describes a complication related to iatrogenic tooth ankylosis and the measures taken to address it.

INTRODUCTION

A 13-year-old male with a history of CCD reported to the Orthodontic Clinic for evaluation. The facial analysis showed midfacial hypoplasia, concave profile, and retrusive lips. Intraoral assessment demonstrated a permanent dentition with 4 erupted teeth in the maxillary arch and 7 in the mandibular arch, with a malocclusion classification of Angle Class III molar and bilateral posterior crossbite ***(Figure 1 a,b,c,d,e)***.

Radiographically, the panoramic x-ray revealed a congenially missing lower right central incisor, multiple teeth with failure of eruption, including upper second premolars and all the maxillary anterior teeth from canine to canine. The lateral cephalometric x-ray revealed a Skeletal Class III with a horizontal growth pattern and normally inclined lower incisors.

MATERIALS AND METHODS

During the initial visit, diagnostic records were obtained, including intraoral and extraoral photographs, lateral cephalometric, panoramic, and limited-field cone beam CT (CBCT) radiographs ***(Figure 2 a,b)***. The treatment protocol developed involved an orthodontic traction phase to deliver the anterior teeth into the arch and an orthodontic phase to optimize dental alignment prior to surgical intervention.

Surgical exposure involved bonding a gold chain to the

six impacted maxillary teeth, followed by initiating orthodontic traction. A palatal-labial bar with various attachment points and hooks was constructed ***(Figure 3 a,b,c)***. This step was taken to begin the orthodontic movement of all the anterior teeth. Throughout the traction process, modifications were made to the appliance to accommodate the varying eruptions.

After achieving full delivery of all anterior teeth with subsequent bonding, orthodontic treatment was aimed at alignment and arch coordination for eventual orthognathic surgery. A LeFort I osteotomy was performed with 6 mm of maxillary advancement. Once the surgical splint was removed, further orthodontic intervention was needed to establish an ideal occlusion and esthetics.

DISCUSSION

Cleidocranial dysplasia (CCD) is a rare congenital bone disorder with an autosomal dominant pattern of inheritance, with a prevalence of 1 in one million individuals. [1] This syndrome involves disturbances in the growth of the cranial vault bones, clavicles, maxilla, and nasal and lachrymal bones with a wide variation of expressivity. Clavicle hypoplasia, cervical elongation, and a sagittal underdeveloped results in the characteristically sunken, midface hypoplastic appearance. [2] Skeletally, patients tend to have a Class III pattern due to maxillary hypoplasia related to a shortened anterior cranial base and a brachycephalic growth pattern with a reduced lower facial third. [3] The dental characteristics in patients with CCD include over-retained deciduous and supernumerary teeth that displace the developing permanent teeth and obstruct their eruption, resulting in multiple impacted permanent teeth and severe malocclusion. Although dental development is delayed, there is a spontaneous eruption of both jaws' permanent first and second molars. Dental anomalies are also present, including hypoplastic enamel, dilacerations, microdontia, and germination. [4]

Our patient's facial analysis showed midface hypoplasia consistent with a Class III skeletal pattern and a brachycephalic growth type. Intraorally, Angle Class III molar classification was noted with upper premolars and anterior teeth impacted. The typical clinical examination and radiographic features present confirmed a cleidocranial dysplasia diagnosis. To render patient care, the following treatment objectives were established: 1) extract supernumerary teeth to provide a path of eruption for the permanent teeth, 2) deliver impacted permanent dentition through orthodontic traction, 3) orthodontically prepare dentition for sagittal correction with orthognathic surgery. The

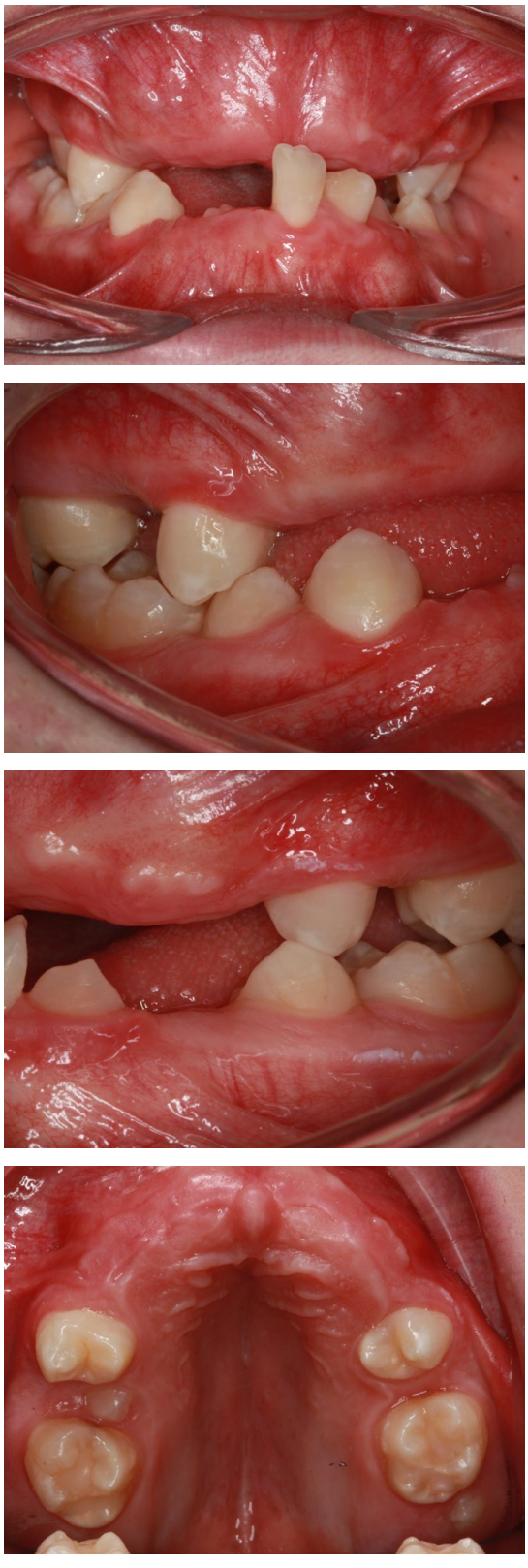


Figure 1 (a,b,c,d) Initial intraoral photographs reveal multiple unerupted teeth in both maxillary and mandibular arches.

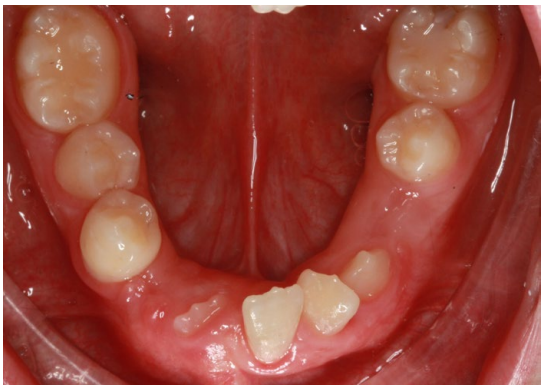


Figure 1 (e) Initial intraoral photographs reveal multiple unerupted teeth in both maxillary and mandibular arches.

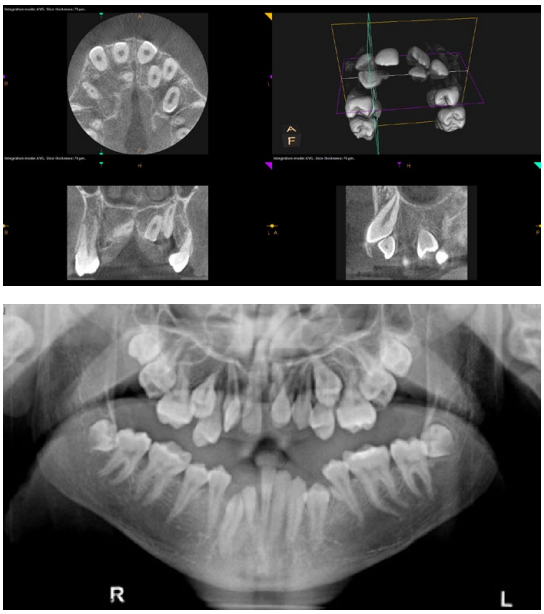


Figure 2 (a,b) Maxillary CBCT and panoramic radiograph showing the impacted dentition in both arches.

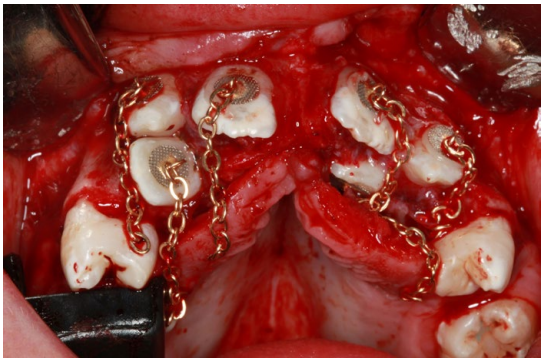


Figure 3 (a) Surgical exposure with a gold chain bonded to all impacted teeth. A palatal-lingual bar with multiple hooks is used for the surgical traction of the impacted teeth.

treatment plan was divided into two phases. The first phase focused on delivering the impacted maxillary teeth into the arch. The second phase involved orthodontic preparation for maxillary advancement and post-surgical finishing.

Although the literature on managing patients with CCD is scarce, the two best-known orthodontic-surgical regimens are the Toronto-Melbourne and Jerusalem approach. [5] In this case, the Jerusalem approach was followed due to the patient's age and clinical presentation at evaluation. Per protocol, all of the supernumerary teeth were extracted, and permanent incisors were surgically exposed. A palatal-labial bar with soldered hooks was fabricated using 036'' stainless steel round wire and delivered before the surgical exposure appointment. This heavy, incisor erupting appliance provided the necessary anchorage and extrusive force to further erupt the impacted teeth into the arch. [6]. As the teeth were being moved into position with orthodontic traction, the palatal-labial bar had to be refabricated multiple times to accommodate all the erupting incisors. Once delivered into the arch, the teeth were progressively bonded using 22-slot brackets and aligned with orthodontic archwires.

After proper maxilla-mandibular arch coordination was achieved, the initially presented skeletal discrepancy became more prominent and consistent with the diagnosis. Since the orthodontic traction phase took multiple years, the patient had reached the skeletal maturity needed to correct his sagittal discrepancy. [7] A Le Fort I osteotomy was performed, with a 6mm maxillary advancement retained with bilateral surgical plates. Immediate post-surgical occlusion demonstrated positive overbite and overjet and improved facial convexity.

Surgical correction of the malocclusion resulted in favorable esthetics; however, complications include numbness, infection, iatrogenic tooth ankylosis from manipulation or screw perforation, etc. [8] During the finishing phase of the orthodontic treatment, as

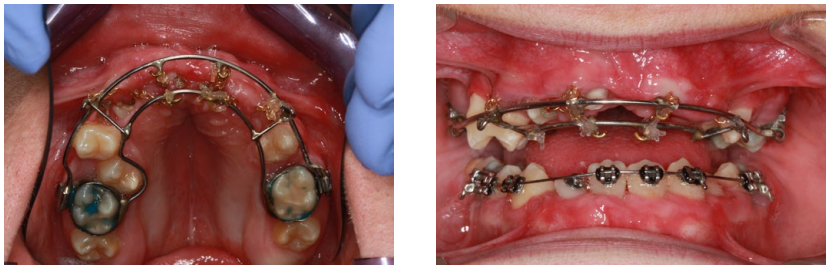


Figure 3 (b,c) Surgical exposure with a gold chain bonded to all impacted teeth. A palatal-lingual bar with multiple hooks is used for the surgical traction of the impacted teeth.

an extrusive movement was attempted on the maxillary right canine, an upward cant was developed in the area. A CBCT radiograph was taken, revealing root perforation with a surgical screw ***(Figure 4 a,b)***. Although the screw was removed, the tooth was deemed helpless, and extraction with implant replacement was recommended. Due to socio-economic circumstances, this treatment option was declined, and a removable prosthesis was inserted ***(Figure 5 a,b,c)***. [1]

CONCLUSION

The surgical and orthodontic techniques involved in the dental management of CCD are demanding in diagnosis, treatment planning, and clinical management. Thus, to achieve the best possible result, multidisciplinary cooperation between surgery, orthodontics, and even prosthodontics is required. [9] The orthodontic treatment in these cases is expected to be lengthy; this patient was in treatment for 6 years, reinforcing the importance of monitoring and maintaining excellent oral hygiene throughout.

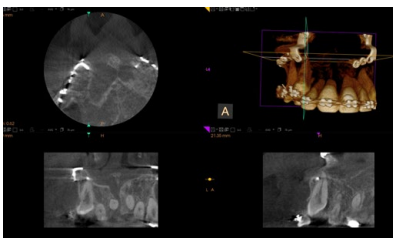


Figure 4 (a) CBCT reveals the screw perforating the root of the upper right canine in the apical third. A maxillary upward occlusal cant developed on the right side.

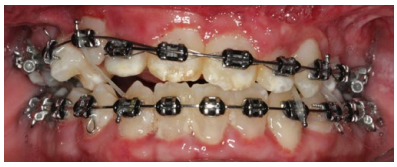
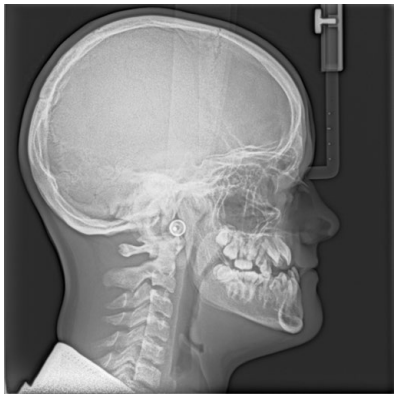


Figure 4 (b) CBCT reveals the screw perforating the root of the upper right canine in the apical third. A maxillary upward occlusal cant developed on the right side.



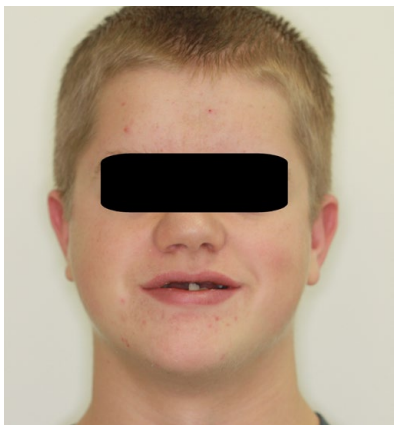


Figure 5 (a,b) Lateral cephalometric radiographs and smile frontal view before and after treatment.

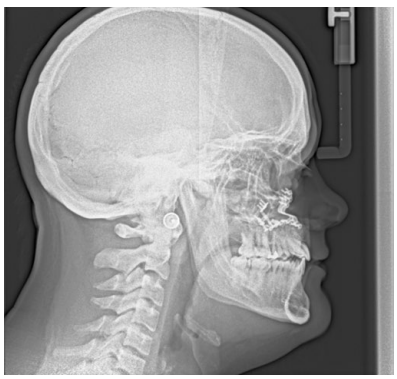


Figure 5 (c) Lateral cephalometric radiographs and smile frontal view before and after treatment.

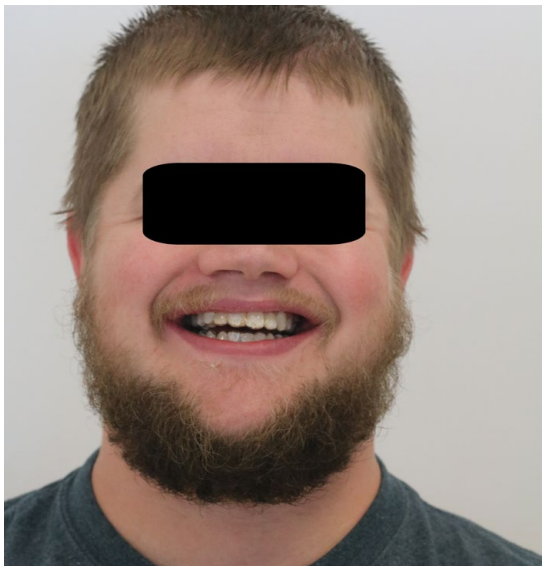


Figure 5 (d) Lateral cephalometric radiographs and smile frontal view before and after treatment.

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RESEARCH CORNER

"To date, we have described nearly a dozen new genes for CLP and three for CFM."

INTERDISCIPLINARY INTERACTIONS DRIVE A TRANSLATIONAL RESEARCH CAREER

TIMOTHY COX
UNITED STATES

Although technically trained as a basic researcher (with emphasis in genetics and developmental biology), much of my career has been centered on biomedical and translational research. The first major career-defining event occurred during my PhD nearly 30 years ago. I sat eagerly in the clinic ready to accept a freshly drawn iliac bone marrow sample from an elderly gentleman with sideroblastic anemia for processing. A few months later, I had discovered the gene – and specific genetic mutation - causing his condition which remarkably pointed to a simple, specific, and effective vitamin supplementation to boost the activity of the defective enzyme and completely alleviate his symptoms. This was all before we had the human genome sequence available to us! Excited by the potential for patient impact, I shifted my interests to more challenging endeavors – understanding the basis of craniofacial birth defects and hopefully one day improving clinical outcomes through early interventions (based on genetics) to prevent or reduce the severity of the condition.

When I began my own research team, I was fortunate to have the Australian Craniofacial Unit, under the esteemed leadership of David David (ISCFS Past President), just down the road from my lab. David's vast surgical experience and passion, supplemented by the expertise and drive of Peter Anderson (ISCFS member) and the pioneering Computed Tomography work of David Netherway, provided a wealth of information and resources to establish a unique research portfolio. I realized then that quantitative 3D imaging (CT or microCT) was lacking in the field of developmental biology and birth defects research using animal models. Thankfully, a multi-Institutional core facility had just purchased a desktop microCT, and from there it became a key part of my research program. As a researcher, however, one of my most impactful experiences came from being asked to accompany the ACU team on a surgical mission to Indonesia, experiencing the significant burden of patients and their families when care was not readily available. At the same time, I saw the wealth of opportunities for impactful long-

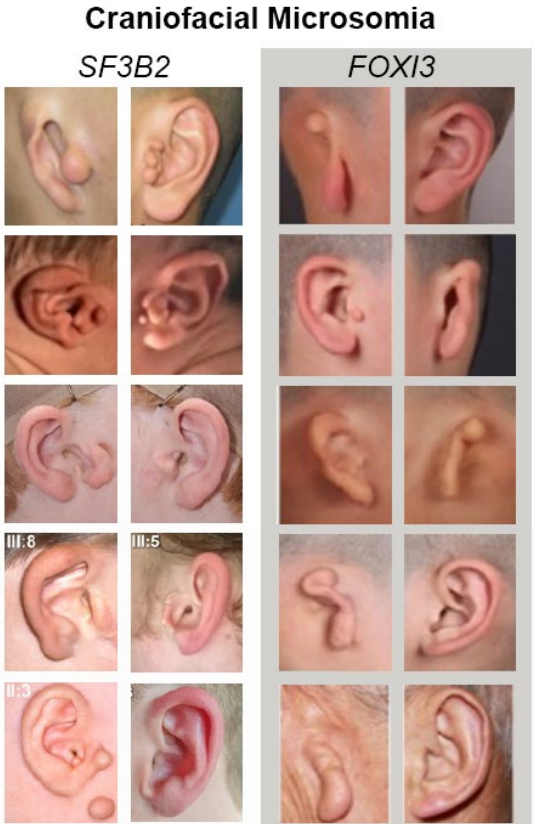

Figure 1: Identification of new genes causing craniofacial microsomia is beginning to reveal distinct clinal spectra characteristic of each gene. Left panel – auricular presentations associated with SF3B2 mutations. Right panel – auricular presentations associated with FOXI3 mutations.

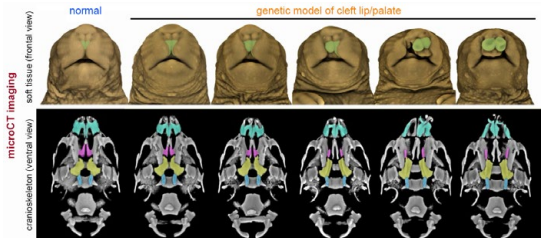

Figure 2: Mouse models of cleft lip/palate are starting to illuminate the mechanisms contributing to clinical variability. MicroCT imaging of perinatal mice. Top panel – soft tissue rendering. Medionasal (philtral soft tissue) shown in pale green; Bottom panel – cranioskeletal rendering from the same specimens as in the top panel. Premaxilla (light blue), palatine processes (pink), palatal bone (yellow), basal pterygoids (royal blue). The left-most image is of a normal (wildtype) mouse; On the r of this are five separate, genetically identical mice (i.e., carrying the same genetic mutation) displaying different severities of cleft lip and cleft palate – from a subclinical presentation to bilateral CLP.

term research. And many of my early research questions were driven by discussions with the surgical team members and clinical genetics colleagues – and initially focused on the craniosynostoses.

Years later, I was recruited to Seattle Children's to help build the new Division of Craniofacial Medicine, the academic entity associated with the Craniofacial Center. Over the dozen years there, I found this to be such a dynamic and interactive environment, with regular inspiration coming from meetings with the stellar surgical team members, including Richard Hopper (past ISCFS President), Joe Gruss, and Ray Tse, as well as the clinical geneticists, pediatricians, and speech pathologists. My research focus slowly shifted to disorders of the midface, including cleft lip/palate (CLP) and more recently craniofacial microsomia (CFM), including microtia, where there was much less known about the underlying genetics. These conditions also intrigued me because of the enormous clinical variability and the high proportion of isolated cases with few identified causes. It was, however, the excitement and insight gained from the discussions with the surgical team at both the ACU and subsequently Seattle Children's that prompted me to join ISCFS in time for the Jackson Hole meeting in 2013. I have remained a member ever since, even though my other commitments have meant only being able to attend one other ISCFS meeting since - in Cancun in 2017.

Although I relocated to Kansas City in 2018, again adjacent another very active craniofacial center at Children's Mercy, my own research and network of clinical colleagues has become more international. My team, in partnership with many research and clinical colleagues, has made remarkable inroads over the years into understanding the genes causing these common craniofacial conditions. To date, we have described nearly a dozen new genes for CLP and three for CFM. Notably, even though both conditions are very heterogenous in causation, careful clinical phenotyping has been important for defining the unique phenotypic spectra associated with each gene ***(Figure 1)***. And perhaps more significantly, through combinations of genetics, diet and quantitative 3D imaging of animal models that reproduce all the variability seen in patients ***(Figure 2)***, we are now starting to better understand the factors contributing to this clinical variability and potentially how to modulate the severity of the clinical presentations. And I remain hopeful that in my lifetime we will develop paths for interventional treatments, based on an individual's underlying genetics (i.e., precision medicine approaches), to ameliorate some of the burden of these common facial conditions.

RESIDENTS CORNER

ALGORITHMIC APPROACHES AND PERSONALIZED MEDICINE IN CRANIOSYNOSTOSIS: A NEW ERA

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INTRODUCTION

Craniosynostosis (CS) is characterized by the premature fusion of cranial sutures, which causes skull and facial dysmorphology, vision changes, developmental delays, and elevated risks of intracranial pressure. To date, the only treatment for craniosynostosis is surgery. Treatment can have varied results as cranial growth and molding post-surgery can be unpredictable.

Furthermore, current treatment protocols do not account for individual variations. This one-size-fits-all approach can lead to a spectrum of outcomes, wherein some patients experience optimal recovery while others face complications such as contour irregularities, persistent osseous gaps, or in extreme cases, re-synostosis and elevated intracranial pressure. The outcome variability highlights the need for a more nuanced yet targeted approach to care. Herein, we provide an update on the customization of treatment protocols for patients with craniosynostosis. Such advances are slowly emerging in diagnostic and treatment realms.

COMPUTERIZED PREDICTIVE MODELING

One focus of personalized care in craniosynostosis has been the utilization of artificial intelligence to create predictive models [1, 2]. The CT scan has been leveraged in some machine learning algorithms to improve diagnosis in a subset of craniosynostosis patients, namely those with metopic craniosynostosis, which occupies a large area of controversy in the field due to its spectrum of disease. Notwithstanding, other confirmatory diagnostic modalities have emerged, such as ultrasound and 3D photogrammetry. Confirmation of craniosynostosis has previously relied on traditional fine-cut CT scans which do carry a small but definite risk of radiation exposure and subsequent malignancy. In today's era, 3D photogrammetry has had a surge of interest as a less invasive, safe, and effective alternative to CT scans. [3]

It follows that these less risky diagnostic tools may be incorporated into machine learning. Photogrammetry describes the process of creating 3-dimensional (3D) models from standard 2-dimensional (2D) photographs. This technique captures images of a child's head from multiple angles and produces a detailed anatomical model that not only aids in the early diagnosis of cranial abnormalities but also predicts their post-surgical progression with remarkable precision. One group has highlighted the use of artificial intelligence (AI) and 3D photogrammetry to personalize surgical approaches for patients with craniosynostosis [2, 4]. They have developed a database of images of patients with and without craniosynostosis, both preoperatively and postoperatively, as well as patients with untreated complications from craniosynostosis, including intracranial hypertension. With this diverse set of references, they utilize AI modeling to detect individual, subtle anomalies such as bone shape, thickness, and density, which guides patient management. Additionally, this software enhances post-surgical outcomes by not only improving surgical accuracy but also providing personalized predictions of potential complications, allowing for proactive measures to prevent them.

In recent studies, machine learning has emerged as a valuable tool in evaluating craniosynostosis severity and enhancing predictive modeling for surgical outcomes. In one study of nearly 196 patients with metopic craniosynostosis, machine learning was found to provide a reliable, consistent assessment of severity, outperforming traditional indices [5]. Building on this, another study focused on predictive modeling in spring-mediated cranioplasty (SMC) for non-syndromic sagittal craniosynostosis. Analyzing data from 124 patients, the research team used machine learning to identify variables most predictive of cephalic index (CI) changes after SMC. These findings contribute to a deeper understanding of outcome predictors in cranial surgeries, guiding improved patient care and precision in surgical planning [6].

This preventive approach can be a crucial tool in overcoming one of the major challenges in craniosynostosis surgery. Under this workflow, providers would ideally gain a detailed understanding of each patient's unique anatomy, predict potential complications up to the age of 10, and guide both their surgical approach and post-operative management by combining personalized imaging data with their professional expertise to develop the best plan for each individual patient.

However, while 3D photogrammetry is a rapidly expanding field, some issues persist with reproducibility and standardization. As highlighted by Kurniawan et al, although 3D photogrammetry is promising, previous literature has shown it has been complicated to capture the complex cranial morphology and all intricacies completely. The ERN CRANIO 3D group advocates for a global effort to conduct a standardized protocol to measure cranial and facial shape [3].

PERSONALIZED PHARMACOLOGICAL APPROACHES

As mentioned above, the current standard of care of craniosynostosis involves surgical intervention through calvarial vault remodeling, which is fraught with variable outcomes and potential complications [7]. Molecular therapy is not only targeting the abrogation of premature suture closure, but also aimed towards mitigating or correcting iatrogenic aspects of care, such as osseous gaps that result from vault surgery. While we will touch on the pharmacologic and biological targets, we will emphasize the technological advancements in biomaterials and tissue engineering used in pediatric skull reconstruction.

As highlighted by Rachwalski et al., recent literature has focused on identifying pharmacological interventions to address the development of craniosynostosis [8]. One promising target is via the targeting of fibroblast growth factor receptors (FGF/FGFR). The FGF/FGFR family comprises twenty-two ligands that play a role in many biological processes, including bone development. When there are mutations in FGFR1, FGFR2, or FGFR3, there is unregulated FGF signaling which leads to the premature suture closure. FGF/FGFR which plays a key role in osteogenesis and has been specifically implicated in craniosynostosis [9]. Researchers have explored strategies to inhibit FGF/FGFR to disrupt its downstream signaling cascade. For example, Tanimoto et. al found that a point mutation of S252W was implicated in the pathogenesis of Apert Syndrome, by inducing an overactive FGFR2 resulting in the development of craniosynostosis. It follows that a soluble FGFR2 with Ser252TRP mutation was found to inhibit osteoblastic differentiation and partially prevent Apert syndrome in a mouse model [10]. Additionally, Eswarakumar found that attenuation of the FGFR signaling pathways has led to prevent premature suture fusion. By selectively uncoupling the docking protein, FRS2α and activated FGFR2 they found this led to normal skull development in

a Crouzon mouse model without negatively impacting normal skull development [11]. Aside from FGF-FGFR targeting, many recent studies have revealed various attempts to target other molecular pathways that may serve as pharmacological treatments for craniosynostosis. For example, Noggin, a BMP antagonist, has been highlighted as another potential therapeutic target. Noggin has been found in patent suture, but not fused, cranial and FGF/FGFR signaling has been found to suppress Noggin expression [12]. Shen et. al. found when recombinant human noggin was applied to FGFR craniosynostosis models, the amount of premature sutural synostosis was reduced. Additionally, Pribadi et. al, found that KDM6A and KDM6B, which are demethylases and known promoters of osteogenesis, could be potential therapeutic targets for craniosynostosis. In their study, they applied GSK-J4, a pharmacological inhibitor of KDM6A and KDM6B and found that this led to decreased osteogenic differentiation and reduced bone mineralization. In vivo, they found the utility of GSK-J4 as therapeutic treatment prevented the fusion of coronal sutures [13]. As different molecular mechanisms have been identified in various clinical manifestations of craniosynostosis, pharmacologic intervention is one way to personalize the treatment of craniosynostosis for individuals.

Although promising, the effectiveness and safety of these treatments for craniosynostosis in humans remain uncertain. While numerous in vitro and some in vivo animal studies have shown promise in targeting various pathways, these have not yet demonstrated long term efficacy and biosafety [8]. According to the FDA, advancing through clinical trials from Phase I to Phase III can take up to 14 years, with many drugs failing due to difficulties in translating results from animal models to humans.[14] While pharmacological agents hold promise, significant uncertainties remain around timelines and the ultimate balance of risks and benefits. The lengthy and costly process, combined with limited success rates, highlights the challenges in developing safe and effective treatments.

TISSUE AND BONE ENGINEERING FOR OSSEOUS DEFECTS

Extensive research is underway to develop personalized treatment strategies for CS involving creating new biomaterials and production processes for bone tissue engineering. Patients with syndromic craniosynostosis tend to have challenging reconstructions due to more severe deformities. Therefore, syndromic patients are reported to have greater reoperation requirements [15]. Personalized surgical planning may hold significant potential here to enhance outcomes [16].

Tissue engineering has been conceptualized as a CS treatment modality to address the significant drawbacks of using autologous or allogeneic implants which can result in poor long-term outcomes in pediatric patients, such as infection, inflammation, or failure [16]. Tissue engineering approaches combine three main components: scaffolds, biomolecules (such as osteogenic factors and other macromolecules), and stem cell therapy [17]. These components work together to meet the essential requirements of an ideal bone regenerative strategy. To achieve these goals, the designed scaffolds must meet various requirements, including specific chemical, physical, and biological properties.

Three-dimensional printed scaffolds have been widely studied as a tool in personalized medicine. Two main strategies are employed: a conductive approach, which provides passive 3D support for cell attachment, migration, and differentiation; and an inductive approach, which incorporates bioactive signals to actively guide cellular responses. Various biomaterials and bioactive molecules have been examined to optimize scaffold performance. Ceramics and polymers, for example, have been studied to improve the anatomical and physiological success of these scaffolds. Polymeric materials, both synthetic and natural, support cell adhesion and proliferation but lack sufficient osseo-conductivity and mechanical strength [18]. In contrast, bioactive ceramics, such as widely used hydroxyapatite, provide excellent osseo-conduction and promote bone healing, though their degradation rates are often less than ideal. Additionally, investigators have focused on integrating bioactive molecules, such as BMP-2, FGF, and TGF-B, to enhance the functionality of 3D-printed implants [18].

In terms of cell therapy, many investigators are harnessing the osteogenic and immunomodulatory features of mesenchymal stem cells to alter suture biology [17]. For example, one group studied the use of autologous mesenchymal stem cells and TGFB3 during osteotomy in rats with craniosynostosis. They observed ossification and synostosis after suture regeneration, concluding that this approach could reduce surgical trauma in craniosynostosis procedures [19]. Gli1+ suture stem cells may also serve a role in the development of craniosynostosis. Previous studies have shown that the loss of Gli1+ suture stem cells may lead to premature fusion of coronal sutures [20]. Additionally, recent data has revealed that the implantation of Gli1+ MSCs

after the removal of fused sutures demonstrated the restoration of suture patency, and normalized skull shape and neurocognitive function [21]. Finally, another potential stem cell-based treatment involves CD51+;CD200+ and their potential to regenerate cranial sutures. One group found that the transplantation of CD51+;CD200+ stem cells with Wnt3a following suturectomy prevented re-synostosis [22]. Aside from CD51+;CD200+ stem cells, other mesenchymal stem cells such as Axin2+, Prrx1+ and Ctsk+ cells can regenerate cranial sutures as well and hold potential for treatment and management in craniosynostosis [17]. These advances in stem cell-based therapies offer a promising pathway for managing craniosynostosis by utilizing the regenerative potential of mesenchymal stem cell populations to regenerate sutures and minimize surgical intervention.

APPLICATION TO CLINICAL PRACTICE

An ideal treatment plan for congenital bone developmental defects must meet numerous criteria to restore skeletal functionality while allowing for normal craniofacial development. This is particularly important in treating craniosynostosis. In this scenario, surgery for bone reconstruction must address the need to prevent premature suture fusion while also permitting proper braincase enlargement and harmonious craniofacial development.

Furthermore, despite significant progress in adult craniofacial bone tissue engineering, optimization for use in pediatric patients has yet to be achieved. A personalized approach is crucial for treating pediatric patients, as it must account for multiple factors, including reduced bone thickness, the decreased osteo-inductive potential of the dura mater after twelve months, and the growth and development of the craniofacial skeleton, which often necessitates multiple surgeries.

Personalized medicine in craniosynostosis as whole, while promising, also presents significant challenges. For example, although AI might enhance access to care, it can unintentionally worsen existing disparities. Many AI-driven clinical studies have been conducted in high-income or upper-middle-income countries, often excluding patients from low-income regions and their unique medical contexts [23]. Additionally, personalized treatments for craniosynostosis are currently available at only a limited number of institutions with access to these advanced tools, limiting these options to patients who can reach these facilities. This disparity leaves patients without access to such institutions at a disadvantage, unable to benefit from these specialized treatments. Finally, AI algorithms depend on data provided by humans, and if this data reflects biases in training, the resulting algorithms may reinforce these biases, leading to unequal outcomes across patient groups [24]. For example, recent research has highlighted that certain AI systems exhibit higher error rates in accurately identifying gender among individuals with darker skin tones compared to those with lighter-skin, with the greatest discrepancies observed in darker-skinned women. This issue is especially critical in photo-based AI applications, such as those used in craniofacial surgical planning, where such biases can result in misdiagnoses and suboptimal management, potentially compromising patient outcomes [25].

Another key consideration in applying personalized medicine to clinical practice is the regulation of AI-based approaches in pediatric care. While the FDA has approved over 1,000 AI-integrated medical devices since 1995, the surge in regulatory submissions has been remarkable [26]. Key issues in AI implementation include the rapid evolution of AI models, the challenges of assessing ongoing safety, and ensuring that AI improves health outcomes without widening existing health disparities [26].

In pediatric craniosynostosis, AI studies often use different metrics and input data, resulting in variability that complicates high-quality, comparative analyses and impacts consistency in patient care [27]. The integration of pediatric patient data also raises concerns around biosecurity and the potential for security breaches [28]. Recent studies have revealed that patients express "algorithm aversion," resisting AI's role in diagnostic decisions, which can have negative outcomes [29]. Given AI's complex potential in healthcare, robust oversight and regulation will be essential to ensure safety, efficiency, and consistency in the healthcare system.

CONCLUSION

Despite the rising incidence of craniosynostosis, management has remained mostly the same with surgery maintained as the gold standard. However, patients with individual variations or those with syndromic craniosynostosis tend to have complex post-operative complications. With the current state of artificial intelligence and digital medicine, we strive to better understand the role personalized medicine can play in craniosynostosis. The emergence of algorithm-driven, patient-specific approaches has the potential to significantly reduce post-operative complications in craniosynostosis and improve overall patient outcomes.

With advances in computer modeling, novel pharmacological targets, and cutting-edge tissue engineering, personalized medicine holds significant potential to enhance patient outcomes, surgical planning and have a transformative impact on clinical management of craniosynostosis. Although many approaches are still in development and not yet standardized, our goal is to contribute to the concerted effort of integrating personalized medicine in the management of craniosynostosis, ultimately advancing treatment for future generations.

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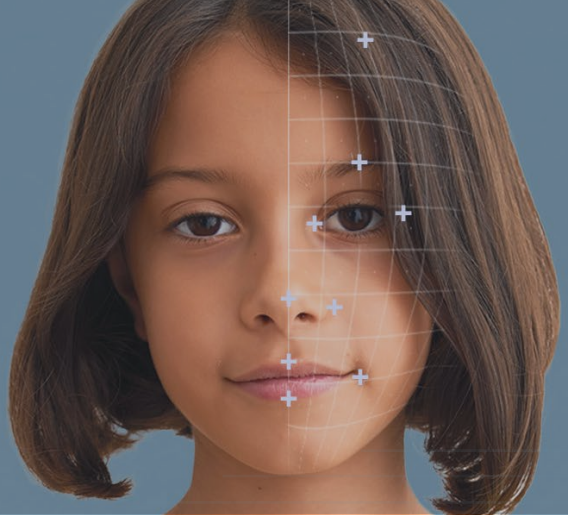

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Assistant Dean, Shanghai 9th People's Hospital

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