

3D CT stereoscopic imaging: observations of the frontal and anterior ethmoid sinuses development from birth to early adulthood*

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Abstract

Objective: Our objective is to provide observations demonstrated with 3Dimensional Computed x-ray Stereoscopic Imaging (3DCTSI) in the evaluation of the anterior ethmoid and frontal sinus development from birth to age 18.

Methods: This is a retrospective evaluation of patient's CT studies performed over a fifteen-year period, reported as normal studies, and included 53 patients (142 sides) from birth to age 18.

Results: At birth, there are two spaces covered by folds, the uncinate and bulla lamellae. The spaces communicate with the Middle Meatus (MM) through the emerging ethmoid infundibulum (EI) and the retrobulbar recess space (RBRS). In the first month after birth, an expansile and breakdown developmental phase blend and continue throughout the growth into the teenage years. The 3D images reveal dark lamellar structures, on the surface of the medial lamina papyracea as well as bridging the broken spatial outlines. The dark lamellae represent the mucosal lamina propria, in unossified lamellae and are the origin of permanent spatial walls. From ages 4 to 18 years, initially, the frontal recess (FR) and later the MM penetrate into the cancellous frontal bone creating the frontal Sinus (FS), the frontal septum (FS), Inter-Frontal Sinus Septal Cell (IFSSC), as well as the Fronto-Ethmoidal and Frontal Bulla Spaces.

Conclusion: 3DCTSI is the first intuitive imaging modality to reveal the microanatomical development of the anterior ethmoid and frontal sinus anatomy.

Key words: ethmoid sinus development, frontal sinus development, frontal sinus drainage pathway, 3-dimensional CT stereo-scopic imaging

Introduction

Several luminaries have reported on the early development and structural variability of the nasal cavity and paranasal sinuses based on their cadaveric dissections and observations from the surgeries they performed⁽¹⁻¹²⁾.

The previous publications provided a baseline for the emerging field of nasal and sinus surgery. Given the demands of Functional Endoscopic Sinus Surgery (FESS) and with significant improvements in imaging technology, interest in understanding

the detailed regional anatomy, especially the frontal-ethmoidal anatomy, remains high and is the topic of several recent reports⁽¹³⁻³¹⁾. Improved 3D imaging has provided new information, which highlights the detailed anatomy of the uncinate process (UP) and ethmoid bulla (EB). This has led to clarifying nomenclature, which is used in this paper⁽²⁹⁻³¹⁾.

However, despite the advances made in endoscopic and imaging technology, the highly compartmentalized nature of the

ethmoid and frontal sinus development remains unexplained, largely due to the lack of anatomical specimens, as well as the lack of indications for the use of imaging to study the sinus development at various ages.

Developmental changes, however, have been studied in nonhuman mammalian species⁽³⁵⁻⁴⁰⁾. This information can be correlated with the human microanatomy demonstrated on 3DCT Stereoscopic Imaging (3DCTSI), which, when necessary, can be augmented with CT multiplanar reconstruction imaging⁽³¹⁻³⁴⁾. Our study focuses on patients ranging in age from birth to 18 years of age, a dynamic period in sinus development⁽²²⁾. The detailed anatomy is illustrated and findings are compared to previous reports in the literature. See Table 1 for annotations.

Materials and methods

Imaging equipment

Axial CT scans were performed on a Siemens Flash or Force 125 slice CT scanner using the following parameters: slice thickness less than 0.75 mm, field of view 14cm, 140mA, 120 kV and a pitch of 0.9.

Studies were performed without administration of intravenous contrast material.

The CT scanners provide density measurements in Hounsfield Units (HU). The range of the density measurements extend from -1000HU for air; 0HU for water; and +3000HU for solid bone. Our control values for sinus tissue density measures were air -1000HU; soft tissue ranging from (-138 to +28HU); MT cartilage/bone (+300 to +500HU); cancellous bone in the frontal diploe (+250 to +720HU); frontal cortex bone (+1150 to +1750HU). On 3D images, low density membranes (< 0HU) appear as dark lamellae, as described below.

An advanced evolution of the Dextroscope imaging device was used to create 3D CT Stereoscopic Imaging displays (3DCTSI) from the original CT data. The device provides “en bloc” 3D display of the imaging data, with the capability of a scrolling removal of the image data in the axial, coronal and sagittal planes. It also has the ability to scroll into the imaging volume in a planar view, which is adjustable to view the image volume at any angle and reveal the anatomy from any obliquity. The device has a virtual surgery capability to remove structures, which obstruct the view of specific anatomic detail. It also has a “replace function” tool to restore inadvertently removed anatomy.

Source of information

The following study, approved by The Johns Hopkins Medical Institutions IRB, is a retrospective study performed on de-identified CT data (IRB00224384). All CT scans were ordered by the patient's physicians. Access to personal information which included the reason for ordering the scans was denied to the current investigators, due to US HIPAA laws.

Table 1. List of annotations.

Annotations	Definitions	Annotations	Definitions
Lamellae		Landmarks	
BaLa (MTBL)	Basal Lamella Middle Turbinate	MT	Middle Turbinate
BL	Bulla Lamella	TUP	Turbinal Uncinate Process
FPM	Frontal Process Maxilla	UL	Uncinate Lamella
FSS	Frontal Sinus Septum	UP	Uncinate Process
LP	Lamina Papyracea		
Spaces			
AES	Anterior Ethmoid Sinus	IFSSC	Inter Frontal Sinus Septal Cell
EB/B	Ethmoid Bulla	ISEUP	Infundibular Space Ethmoid Uncinate Process
EI	Ethmoidal Infundibulum	MS/M	Maxillary Sinus
FR	Frontal Recess	PES	Posterior Ethmoid Sinus
FS	Frontal Sinus	TI	Turbinal Infundibulum
MM	Middle Meatus		
Miscellaneous			
CT	Computed X-ray Tomography	3DCTSI	3D CT Stereoscopic Imaging
MPR/CTMPR	CT Multiplanar Reconstruction		

Only patients with normal sinuses were included: without evidence of trauma, congenital abnormalities, inflammatory or neoplastic pathology. CT data of 53 patients (142 sides) were evaluated. 42 patients had single studies (84 sides); and 11 patients had 2 or more studies, for a total of 29 studies (58 sides).

Results

(See Table 2 for developmental summary)

Three phases are recognized in the development of the anterior ethmoid sinus: 1) the presentation at birth (Figure 1); 2) the first month through 4th year, i.e., “breakdown phase”; and 3) the 4th year to early teenage years, the “rebuilding phase” (Figures 2 – 9). The FS development begins at the age of 3-4 years, with the anterior expansion of the frontal recess (FR) into the cancellous frontal bone (Figures 4-10).

3DCTSI analysis of the anterior ethmoid sinus development: ages birth to 4 years old

Birth to 1 month old

The middle meatus (MM), which is demarcated posteriorly by the Basal Lamella (BaLa) of the middle turbinate (MT), covers

Table 2. Summary of 3DCTSI developmental observations.

3DCTSI Development of the anterior Ethmoid Sinus birth to early teenage years.	
Birth - 1 month.	The middle meatus space covers the uncinate and ethmoid bulla folds. It extends through the hiatus semilunaris and retro-bulla recess to the lamina papyracea, creating two distinct spaces, the ethmoid infundibulum (EI), and the retrobullar recess (RBR) (Figure 1).
1 to 2 months.	The EI groove expands superiorly creating an anterior-superior space covered by a third fold between the uncinate process (UP) and ethmoid bulla (EB). At this point two bony ridges separate the three spaces. In the 2nd month, the two ridges undergo a resorption, the beginning of the breakdown stage, and the beginning of the frontal recess (FR). The space covered by the turbinal uncinate process (TUP), is the turbinal infundibulum (TI) which expands inferiorly into the maxilla, the early maxillary sinus (MS) (Figure 1).
3month - 1 year.	The expansile process increases as does the breakdown of spatial boundaries. Well defined dark outlines appear on the medial wall of the lamina papyracea (LP), which when compared to non-human mammalian species correspond with the mucosal lamina propria, the origin of spatial bony barriers /walls. A similar dark outline is seen along the evolving lamellae of the UP and BL, as well as within the posterior ethmoid sinus (PES) (Figures 2-4).
1 - 4 years.	The “ rebuilding ” process is more prolonged, with evidence seen at three years (Fig. 3) and extending into teenage years. New spatial boundaries/lamellae are created within parallel mucous membranes, recognized as dark lamellae composed of soft tissue with a low (negative) Hounsfield Unit (HU) density (Figures 3-5)
3DCTSI Development of the Frontal Sinus: ages 4 to 18 years old.	
3-5 years.	The FR and MM begin to penetrate anteriorly into the cancellous frontal bone beyond the coronal plane of the FPM. Segmented lamellae within the AES and PES are linked by dark membranous structures which complete the balloon like enclosures (Figures 5- 7).
6-10 years.	The FR spatial expansion into the cancellous frontal bone progresses. The midline cancellous frontal bone is eliminated, as the FSes expand medially and fuse to create the Frontal Sinus Septum (FSS) a midline or off-midline structure (Figure 8).
4-teenage yrs.	The Inter-Frontal Sinus Septal Cell (IFSSC): Bilateral paracentral septations the result of fusion of the antero-superior MT and UP anterior to the enclosed MM within the medial FS. These lamellae also partially fuse with bony grooves along the antero-inferior FS., creating opening(s) in the lamella(e) which provide communication between the FS and the midline space (IFSSC) (Figure 9). The midline space also communicates with the MM bilaterally. The communication is therefore not the result of a diverticulum (18). Bony ridges may adhere to the frontal septum, and on some orthogonal CT planes may falsely appear as IFSSCs (“IFSSC mimics”) (Figure 10). CT MPR can distinguish between this presentation and a true IFSSC and a “IFSSC mimic”.
Early Teens	The Fronto-Ethmoidal and Frontal Bulla Spaces: are created by lamella expanding from the EUP and or the BL into the FS. The 3D images show the transition from soft tissue to bone (Figure 10).

two “hockey sticks shaped folds”, from anterior to posterior: the Uncinate Process (UP) having two components: “pars ascendens” and “pars descendens” and the Ethmoid Bulla (EB) ^(3,12). The MM extends from the middle turbinate medially to the lamina papyracea (LP) laterally, penetrating the furrows between the uncinate lamella (UL) and bulla lamella (BL), anteriorly; as well as between the BL and the middle turbinate basal lamella (BaLa), posteriorly. The anterior furrow is the precursor of the hiatus semilunaris and the ethmoid infundibulum (EI) ^(4,5). It communicates with the space being enclosed anteriorly by the ethmoid uncinate process (“pars ascendens”/EUP) (previously called the Agger Nasi Cell) or in an alternative designation the Infundibular Space of the Ethmoid Uncinate process (ISEUP) ^(33,34). The posterior furrow is the precursor of the retro-bulla recess space, which will eventually communicate with the emerging EB space. The horizontal portion of the UP is in close spatial relationship with the lacrimal bone and the inferior turbinate, and it visually extends posteriorly to the Posterior Fontanelle (Figure 1) ⁽³³⁻³⁴⁾. The EI extends inferiorly between the turbinal uncinate process and the medial maxillary sinus wall creating the turbinal infundibulum as part of the complex infundibular space and subse-

quently the maxillary sinus (MS) ^(4,7,10,30,31) (Figures 1,2).

1 to 2 months old

The EI furrow expands superiorly and creates an anterior-superior space. A third “fold” is created, which covers this newly created space between the UP and EB. At this point two bony ridges separate the three spaces. Towards the end of the 1st and into the 2nd month the two ridges undergo a resorption creating a single superolateral space, the Frontal Recess. This is, the first sign of the “breakdown stage”, resulting in a single space extending from the upper Middle Turbinate Basal Lamella (BaLa) posteriorly, to the frontal process of maxilla (FPM) plane, anteriorly. The superior unified space is in direct communication with the superior EI and the space outlined by the UP, which at this stage is not enclosed superiorly or posteriorly (Figures 2-4).

3 months to 1 year old

Expansion with individual breakdown of the outlines of anterior ethmoidal spaces continues. Well defined dark outlines appear on the medial wall of the LP, which when compared to non-human mammalian species correspond with the lamina propria

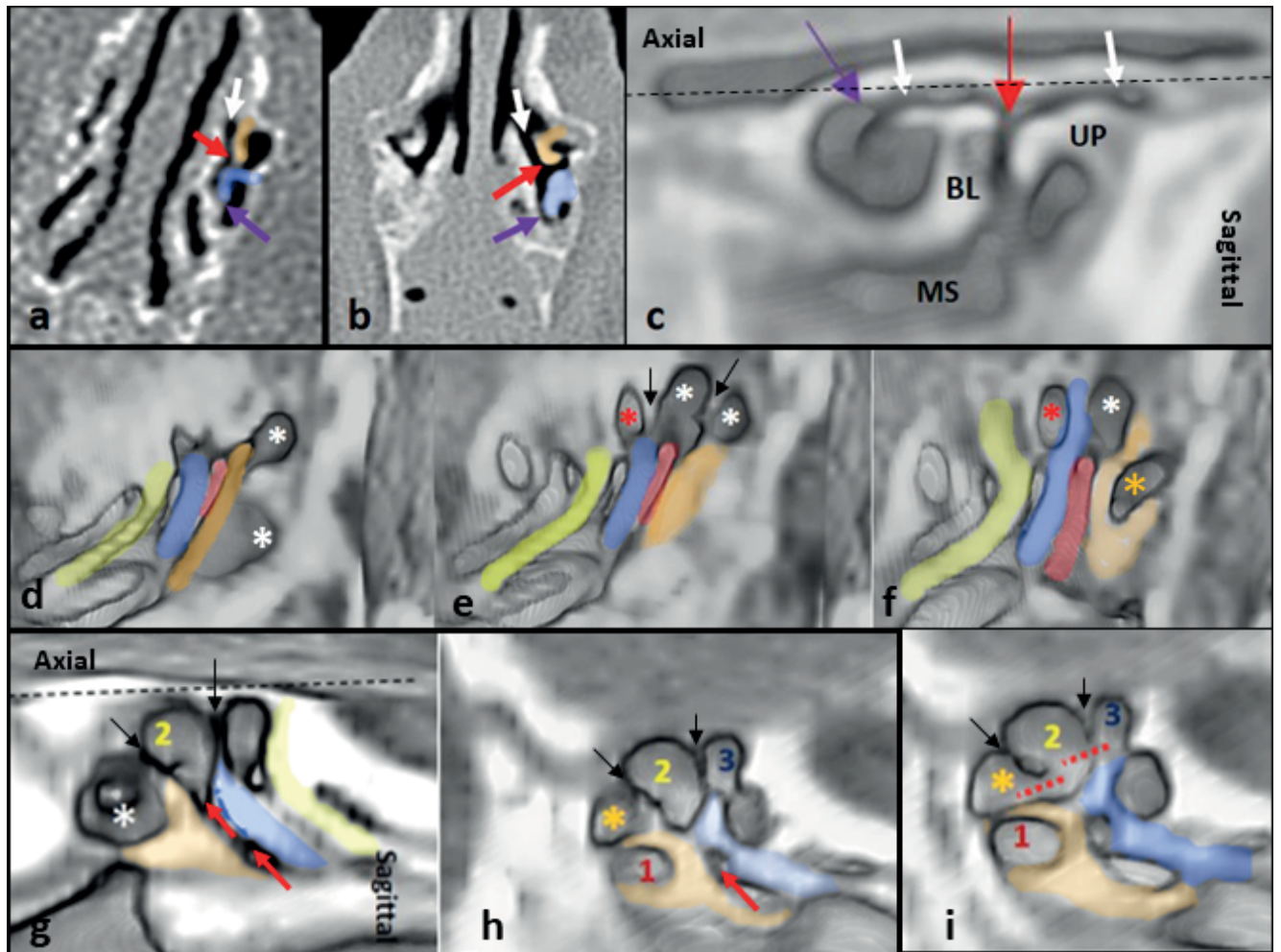


Figure 1. Developmental changes in the lateral nasal wall within the first month of life, as shown in four patients.

a.-c. Axial CT images: figs. (a.) at age 3 days, and (b.), at 11 days; with fig. (c.), 3D oblique sagittal image at 11 days old; viewed from laterally which reveal the MM (white arrows), expanding between the free edge of the Uncinate Lamella (gold outline, UP) and the Bulla Lamella (blue outline, BL) to create the emerging Hiatus Semilunaris and the EI (red arrow). Similarly, the MM expands posteriorly to communicate with the emerging Ethmoid Bulla space (purple arrow). Maxillary Sinus (MS).

d.-f. 3D left sided sagittal images of a 7day old patient, viewed progressively from medial to lateral. They reveal the UP (gold) and the EB (blue) "folds", as well as the anterior rim of the MT Basal Lamella (yellow-green). The Hiatus Semilunaris and EI "groove" in red is between the UP & EB. The RBS is visible between the EB and the MTBL (BaLa). The lateral extension of the MM above the EB and UP creates the respective "pits" (white asterisks) and also the "pit" above the RBS (red asterisk). The space within the outline of the UP is the emerging Infundibular Space, which will become enclosed by the Ethmoid Uncinate Process (IS-EUP) (gold asterisk).

g.-i. 34 d old Infant. Sequential 3D oblique, right sided sagittal images from medial to lateral reveal the UP (gold) and EB (blue) folds, as well as the anterior ridge of the BaLa (yellow-green). The ridges (black arrows) separate the MM evaginations into the LNW, which create the "pits" or "furrows", that become apparent with progressive medial scrolling into the AES (white asterisks). Note the gradual balloon like expansion of the superior EI (red arrows, yellow 2), as well as the appearance of the IS-EUP (red 1), the space above the EUP (gold asterisk) and the space above the EB (3). Note also, the remodeling dissolution of the "dark" cartilaginous ridges, most pronounced in fig. (i.), between the spaces above EUP (gold asterisk), the superior EI (yellow 2) and above EB (3), which is highlighted by the red dotted lines. This reveals the early phase in the creation of a single superior antero-lateral space within the AES, above both IS-EUP and Ethmoid Bulla.

of developing ridges, the origin of spatial bony walls or barriers. A similar dark outline is seen along the margins of the evolving EUP and EB, as well as within the PES. The expansile process is more evident in the AES. The expan-

sion of the antero-superior space, the evolving FR, is in direct communication with the EI, as well as the evolving ISEUP, as the latter lacks complete closure of its superior and posterior walls (Figures 2-4).

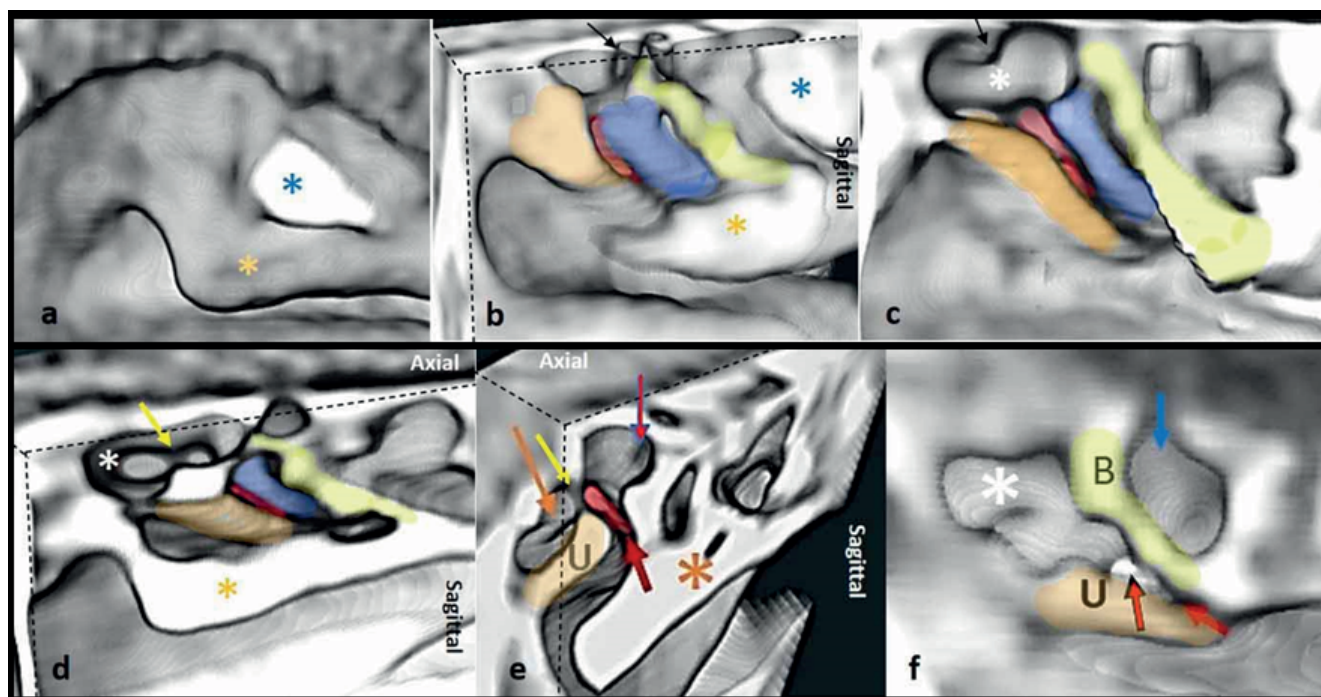


Figure 2. The creation of a single space above the AES folds in a 1 month, 17-day old patient.

a. Sagittal 3D image of the lateral nasal wall after virtual septoplasty. Middle Turbinate (gold asterisk), Superior Turbinate (blue asterisk).

b.-f. Sagittal 3D images of the right nasal cavity and ethmoid sinus at various oblique angles. Note the "folds" of the UP (U, in gold), the Ethmoid Bulla (in blue) and the MT Basal Lamella (yellow-green). In figs. (b., c.) the cartilaginous "ridge" (black arrow), which separates the spaces above the uncinate and ethmoid bulla, is undergoing dissolution as it is remodeled. Also note that the remodeled ridge has a dark contour. The dark density is also evident in figs. (d., e.) at the yellow arrow, which marks the separation of the superior IS-EUP space (gold arrow) from the space above the EI (red outline, red arrow) and the EB (blue outlined red arrow). In figs. (c.-f.) the superior space above the uncinate and bulla folds is a united singular space (white asterisk). The Maxillary sinus opening (black outlined red arrow).

1 to 4 years old

The expansile breakdown of spatial boundaries continues. However, in this age range new structures emerge: indicating a "rebuilding process" whereby new laminae are formed. This rebuilding process is prolonged, with evidence seen at three years (Figure 3) and extending into teenage years (Figures 3-7). In this process, new spatial boundaries/lamellae are created within parallel layers of mucous membranes that we recognize as dark lamellae.

They are composed of soft tissue with a low (negative) HU density. With aging, we see a progressive transition to higher HU densities, finally reaching HU densities in the positive range i.e., the transition to bony density (Figure 7). Specifically, the dark membrane density ranged from (-700 HU to -400 HU) in younger patients, and (-400 HU to 0 HU) in older patients. The HU measurements indicate that the density of the dark outline represents a transition from soft tissue to bone formation.

Our control values were: air -1000HU; soft tissue ranging from (-138 to +28HU); MT cartilage/bone (+300 to +500HU); cancellous bone in the frontal diploe (+250 to +720HU); frontal cortex bone (+1150 to +1750HU). On 3D images this transition is ob-

served as an intact membranous structure, extending between fragmented lamella, as well as a ballooning membrane, creating a space along the dark grooves on the medial bony LP surface (Figures 3-7).

3DCTSI frontal sinus development: ages 4 to 18 years old

3 to 10 years old

In ages 3-5 years old, both the reconfigured antero-superior AES, commonly referred to as the FR, and the MM gradually begin to penetrate the cancellous frontal bone anterior to the coronal plane (posterior surface) of the frontal process of maxilla (FPM) (Figures 3, 4). During this stage the expansion within the AES and the PES continues, and the random disorganized incomplete lamellae become more apparent. The dark membranous structures continue to be present between the incomplete lamellae and appear to merge the segmented lamellae to create expanded "balloon like" spaces in the AES (Figures 3-5). From ages 6-10 years old, the spatial expansion into the cancellous frontal bone progresses. The midline cancellous bone separating the bilateral expanding FS spaces, is ultimately eliminated and the medial borders of the expanding spaces fuse to

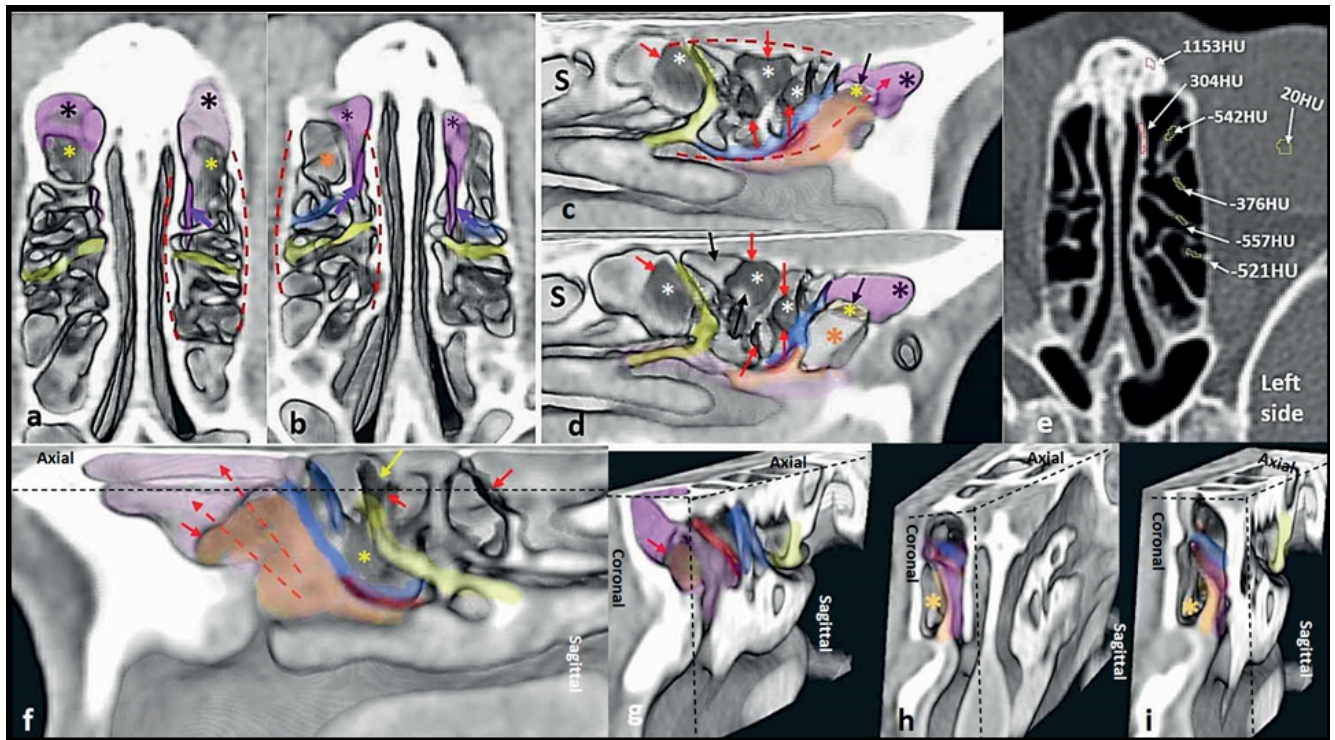


Figure 3. The “rebuilding” of the AES and PES, and the expansion of the FS by the MM in a three years-ten months old patient.

a.-d. 3D axial images (a. superior to b.), and (c., d.) left side 3D sagittal images from medial to lateral reveal the extension and communication of the MM (purple outline and arrows) with and into the FS (black asterisk). On the sagittal images, note the beginning anterior expansion of the EUP (gold) into the FS (purple), and the early expansion of the MM into the FS (red dashed arrow). The bony/cartilaginous architecture within the AES and the PES have an irregular arrangement, without defined spatial structures (within the red curved dashed outlines on fig. c.). Within the “irregularly spaced” ES lamellae, a well-defined dark membranous structure (white asterisks) expands within the borders of well-defined dark “wedgelike” borders within the outline of the LP (red arrows) expanding towards existent lamellae. These changes represent the “rebuilding” process of previously “broken up” spaces and the recreation of the final expanded spaces of the anterior and posterior ethmoid sinuses (yellow asterisks). The continued presence of the well-defined dark “rims” (red arrows) surround the origin of the membranous expansion. Bulla lamella (blue outline); basal lamella (green outline); sphenoid sinus (S).

e. A standard axial CT image in the surface plane of the 3D axial image fig. (b.) Density measures represented in Hounsfield Units point to the fact that the thin dark lamellar outlines have values below the density of soft tissue and water (0HU, here 20HU in mid orbit), and are markedly lower than superior nasal bone (1153HU) and MT cartilage (304HU) densities. It is likely that these lamellae (-376HU to -557HU) are membranous pathways for bony lamellar development.

f.-i. Fig. (f.) 3D sagittal image of the right lateral nasal wall, and figs. (g.- i.) are oblique coronal/sagittal/axial images, all showing the expansion of the MM into the FS. Similar to images a.-d. the expansion of the MM into the FS is highlighted with the purple coloring as well as the dashed red arrows. Also of note are the dark rim outlines (red arrows) establishing the perimeter zones of the membranous expansion (yellow asterisks and yellow arrow).

create the FS Septum (FSS) (Figure 8); The septum may be in the midline, paramedian, or not exist at all, as one expansion takes over and creates the FS with a single communication with the MM and the FR (Figure 8).

11 to 18 years old

Increased FS size is associated with: antero-superior expansion of the MM into the medial FS (Figures 3-5, 8-10), with creation of bony ridges along the floor, the anterior surface and/or along the septum of the FS. Paracentral septations, may also be

present and create the Inter-Frontal Sinus Septal Cells (IFSSC) (Figure 9).

The Inter-Frontal Sinus Septal Cell (IFSSC)

An increased FS space may be accompanied by an antero-superior expansion of the MM into the medial FS (Figures 3, 8, 10). This is observed from age 4 into the teenage years. Given that the MM is bordered medially by the MT and laterally with the UL, the antero-superior extension of the MM into the medial FS, may be associated with antero-superior expansion and fusion of

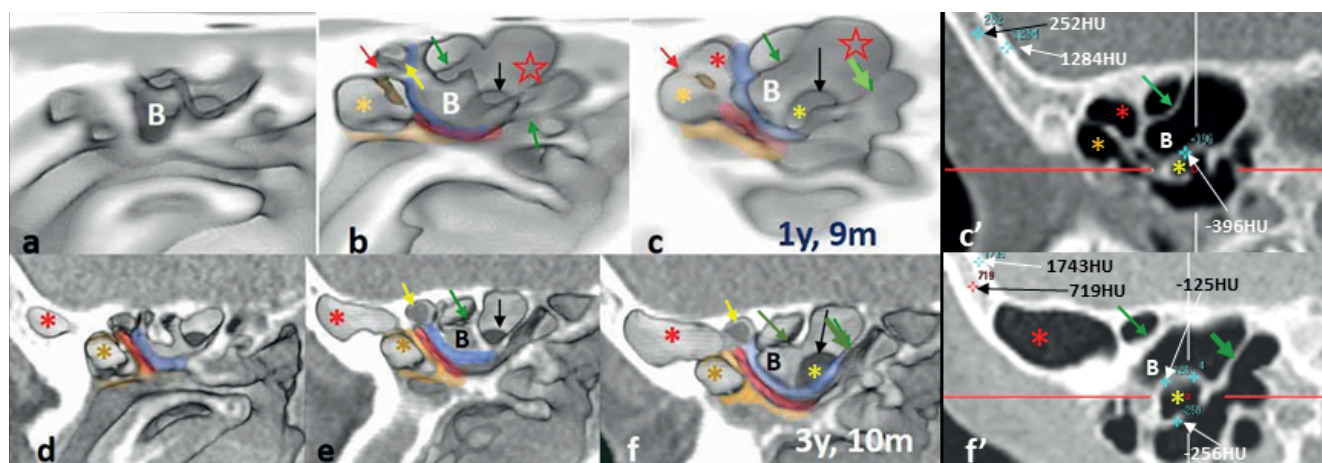


Figure 4. Early Ethmoid Sinus development over a two-year interval.

a.-c'. Right sided 3D sagittal images of a one year and nine months old patient reveals the coexisting developmental expansile/'breakdown' and 'rebuilding stages of the AES and PES with expansion of the ISEUP (gold asterisk), the expansion of the EB (blue outline) and the PES (red star) as well as the beginning recreation of the expanding UP outline (gold outline). Note the distinct oval dark rim (black arrow) within the medial surface of the LP and within the inferior EB/PES appearing to be covered with a thin dark membranous 'film' (yellow asterisk). Similar less defined 'grooves' (green arrows) also noted within the medial surface of the LP in the superior EB region and inferior PES, likely the beginning stages of lamellae/spatial creation.

Fig. (c') is a standard sagittal CT reconstruction image of fig. (c's) surface plane. It reveals the 'grooves' outline, designated by the green arrow in fig. (c). It also demonstrates the ISEUP (gold *), the space above the superior EI (red*), and the outline of the emerging oval space (yellow * in f.), which has a -396HU. Note the positive values of the Frontal Bone and the cancellous bone within the frontal diploe.

d.-f'. 3D sagittal images of the same patient at three years and 7 months of age, reveal the early stages of FS (red asterisk) expansion, the communication between the FS and the EI (red outline), and the established outline of the EUP (gold outline) with an enclosed ISEUP (gold asterisk). Note the distinct dark lamellae in figs. (e., f.) (green arrows) along earlier dark 'grooves' in figs. (b., c.), as well as the creation of what appears as a 'ballooning' space (yellow asterisk) along the inferior border of the EB (B) in figs. (e., f.). The PES spaces are becoming more distinct.

A similar dark membranous shadow is evident within the outline of a SBS in fig. (b) (yellow arrow) which is more defined and nearly spanning the SBS in figs. (e., f.). Note the slight anterior penetration of the FR into the frontal bone (red asterisk) (d.-f.) Ethmoid bulla (B). Fig. (f') is a sagittal standard CT image in the plane of the surface of fig. (f.), revealing the corresponding emerging dark lamellae in figs. (e., f.). Note the less negative HU units outlining the perimeter of the oval space shown in figs. (c., f.), with more pronounced densities in the frontal bone cortex as well as the frontal bone cancellous bone.

the MT and the UL. Not infrequently, the antero-superior fusion of the UL and MT, extends forward as a common lamella to the anterior frontal sinus wall, creating a para-median septation within the FS. This may be unilateral or bilateral. Frequently a bony septal defect is present within the paramedian FS septation (Figure 9).

At times the paracentral septation is noted to fuse with irregular bony ridges arising from the antero-inferior FS, creating apparent bony defects or gaps. Some of these are covered with a dark membranous structure which with aging converts to a bony structure and seals the 'gap'. However, some of these gaps remain unsealed and a communication is created between the ipsilateral FS and the created midline space. When the paracentral septations are bilateral, the midline space – the IFSSC – communicates with the antero-superior MM bilaterally (Figure 9). Bony ridges may adhere to the frontal septum, and on some orthogonal CT planes may falsely appear as IFSSCs (IFSSC mi-

mics) (Figure 10). CT MPR (coronal plane) aids in distinguishing between a true IFSSC and a IFSSC mimic.

The Fronto-Ethmoidal and Frontal Bulla Spaces

Anterior Ethmoid spaces may also expand into the FS. Similarly, lamellae arising from the EB and/or the EUP may expand into the FS, creating a Fronto-Ethmoidal or Frontal Bulla Space. An example of this is a 13-year-old patient, who has a dark lamella expanding from the junction of the UL and BL into the FS. Within the FS the dark outline, which is irregular in appearance creates a space within the FS, potentially communicating with the FS, FR, and ISEUP. It may also develop into a Fronto-Ethmoidal or Frontal Bulla space (Figure 7g-i).

18 years to adulthood

The appearance of supernumerary FS and supraorbital Ethmoid Spaces (cells) were not present in our pediatric population. This

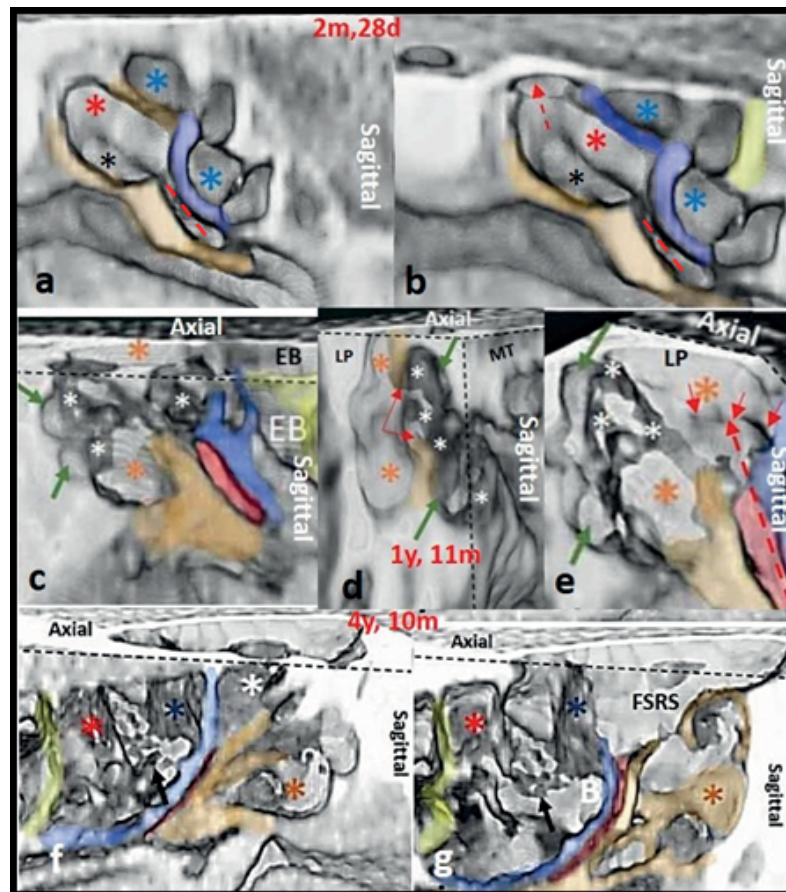


Figure 5. Expansion of ES space(s) and appearance of the "dark lamella", at ages: 2months-28 days; 1 year-11 months; and 4years-10 months.

a., b. 3D right sided sagittal obliques images, reveal the medial surfaces of the UL (gold), and the EB (blue), as well as the MT Basal Lamella (yellow-green). Note the EI (red) and the communication of the EI with a more prominent space between the UL and EB, which appears to be segmented by an oval dark outline (black *). This is likely the origin of a spatial creation and separation between the emerging ISEUP (black asterisk) and the more superior space (red *), the emerging FR. Note the antero-superior extension of the potential FR. The EB space is denoted by blue asterisks.

c.-e. 3D right sided oblique sagittal images in a 1 year, 11 month patient, reveal the medial surface of the UL (gold), BL (blue), and BaLa (yellow-green) folds. All the images reveal the developing medial outline of the UL. Note the "tattered" dark foci (white asterisks) which represent "bony islets" infiltrating the membranous construct of the UL. Note the presence of a larger space between the LP and the UL, best displayed in fig. (d), with two gold asterisks representing a united space between the ISEUP and the FR, at this stage. Also shown is a "gap" in the UL outline (joined red arrows). The space between the MT (MT) and the UL is the MM (green arrows).

f., g. 3D left sided oblique sagittal images in a 4 year, 10 month old patient, showing the medial surface of the UL (gold), BL (blue), and BaLa (yellow-green). The images reveal a more solid "black lamella" area of the LP, between the BaLa and a lamella within the EB space (red asterisk), and on the LP, between the intermediate lamella and the BL (dark blue asterisk). There is also a similar dark area between the BL and UL (white asterisk). These represent a more advanced development in the membranous bony evolution, which creates the LP, as the permanent lateral boundary of the Ethmoid Sinus. Also note the tattered dark foci within the EB space (black asterisk), representing "bony islets" infiltrating the membranous construct of the EB space. ISEUP (gold asterisk); and Frontal Sinus/Frontal Recess Space (FSRS).

is likely due to the fact that additional enlargement of the FS is a prerequisite, and noted to occur beyond the age of 18 years and observed in the adult population^(22-25, 31).

Discussion

Reports on the development of the ES and FS date back to the early 1900s⁽¹⁻¹⁰⁾. Disagreement is reported with respect to time of origin of the FS: Davis stated that the FS is demonstrable near

the end of the first year, as pneumatization gradually extends from the anterior ethmoid sinus into the frontal bone as cancellous bone is resorbed⁽⁹⁾. Shaeffer stated that a frontal sinus is first recognized "at the end of the first year, however, one is certain of its presence by the third year"⁽⁴⁾. There appears to be disagreement regarding end of FS development: Koch reports the end of FS growth to be at age 20⁽²⁴⁾; Stern reports the end of the FS expansion to be at age 40⁽²⁵⁾, while Finby and Kraft

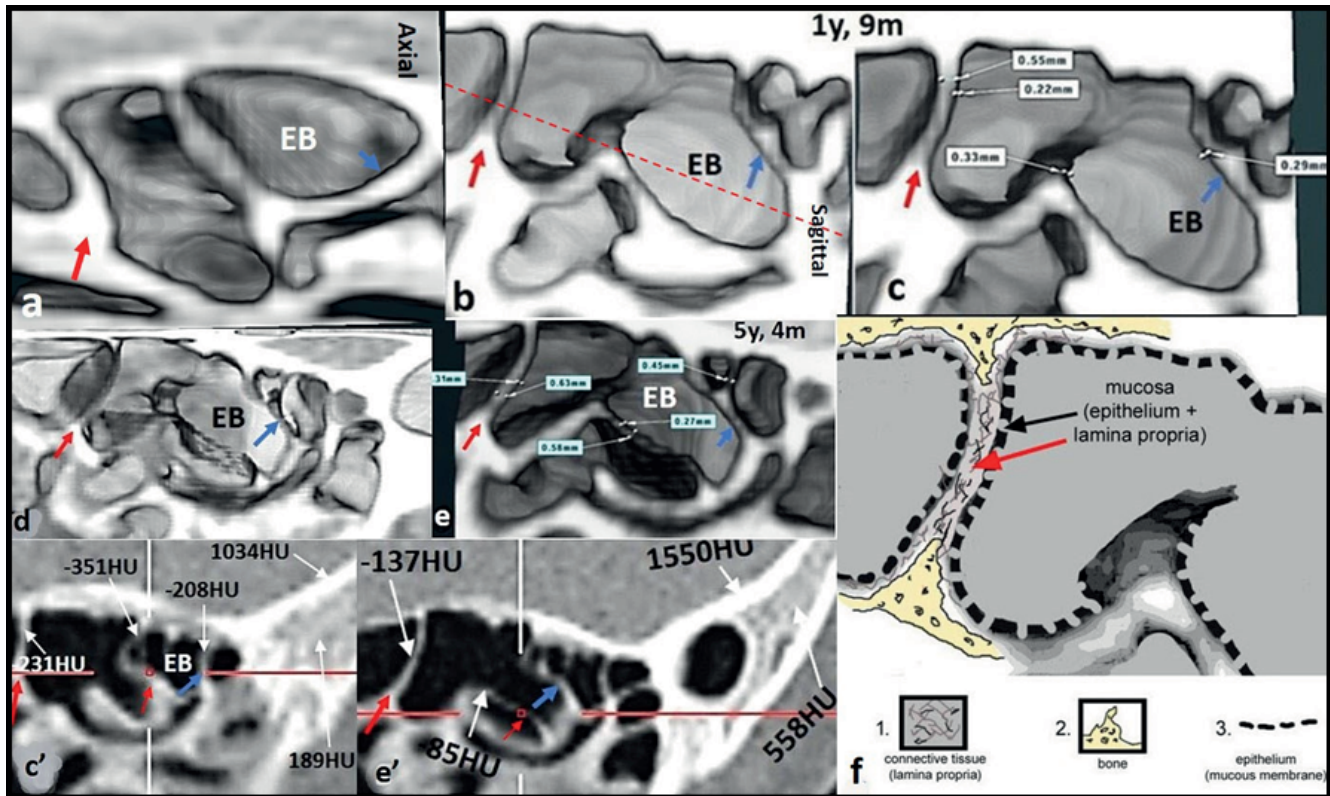


Figure 6. The “dark membranes” and the evolving ES cartilage/bone formation over a three-year, seven-month interval.

a.-c. Left lateral nasal wall of a one year and nine-month-old patient focused on the anterior ES. Note in fig. (a.) a 3D axial image, with its angulation corresponding to the plane of the red dashed line in the sagittal 3D image fig. (b.) showing the anatomy between the BL (blue arrow) and the Basal Lamella (red arrow). Note in fig. (c.) the “dark membranous sheath” highlighted in the slightly magnified fig. (b.) covering the cartilaginous/bony outlines, and “sandwiching” the cut lamellae. Note the “membranes” thickness is approximately 0.22 – 0.33mm. The thickness of the superior MT Basal Lamella is approximately 0.55mm.

d., e. 3D sagittal images of the same patient (fig. e. shown with a darker window with/level to highlight the thickness of “sandwiching” membranes) the at the age of five years and four months. Note the more prominent cartilage/bone anatomy between the Basal Lamella (red arrow) and the BL (blue arrow). The thickness of the Basal Lamella is 0.63 mm.

c': A standard sagittal CT image corresponding to the medial planes of figs. (b., c) reveals the density of the Basal Lamella to be -351HU.

e': A standard sagittal CT image corresponding to the medial plans of figs. (d., e.) show the density of the Basal Lamella to be -135HU, an increase in density over 3y, 7m.

f. A schematic representation of the Basal Lamella in the sagittal plane, represents our interpretation of the tissue layers composing the Basal Lamella. Parallel membranous mucosal epithelia (black arrow, and heavy dashed line), which surround the lamina propria (red arrow, and represented in legend 1.), arise from the lamina papyracea of the AES. Bony islets and osteoblasts from the LP extend into the lamina propria space, which is covered by the parallel mucosal epithelium (legend 3.) represented by legend 2. (yellow outlined area).

Thus, bone is produced on the external surfaces of existing bone, by osteoblasts that migrate to the bone's surface from the periosteum, analogous to intramembranous bone formation. The bony lamellae that separate ethmoid air cells originate from the existent ethmoid surface and invade existing membranous septa (i.e., the “dark membranes”).

The two studies indicate that the “sandwiching dark lamella” with progressively diminishing negative HU measurements suggests that these structures start of as entirely soft tissue and transition into a bony structure as peripheral existing bone invades and replaces the midline soft tissue.

report that FS growth extends beyond age 40⁽²⁶⁾. We limited our evaluation to the “generally accepted” pediatric age i.e., birth to age 18⁽²²⁾.

The literature presents several concepts regarding the origin of the FR. Onodi and Killian refer to the FS as a space in the antero-

superior MM containing the ostium of the FS^(1,2). Schaeffer and Kasper considered the FR to be the origin of the FS^(3,4,6). Van Alyea considered that the FS developed from the frontal recess in the ascending ramus of the middle meatus or the ethmoidal Infundibulum, or from a cell located in or around the infundi-

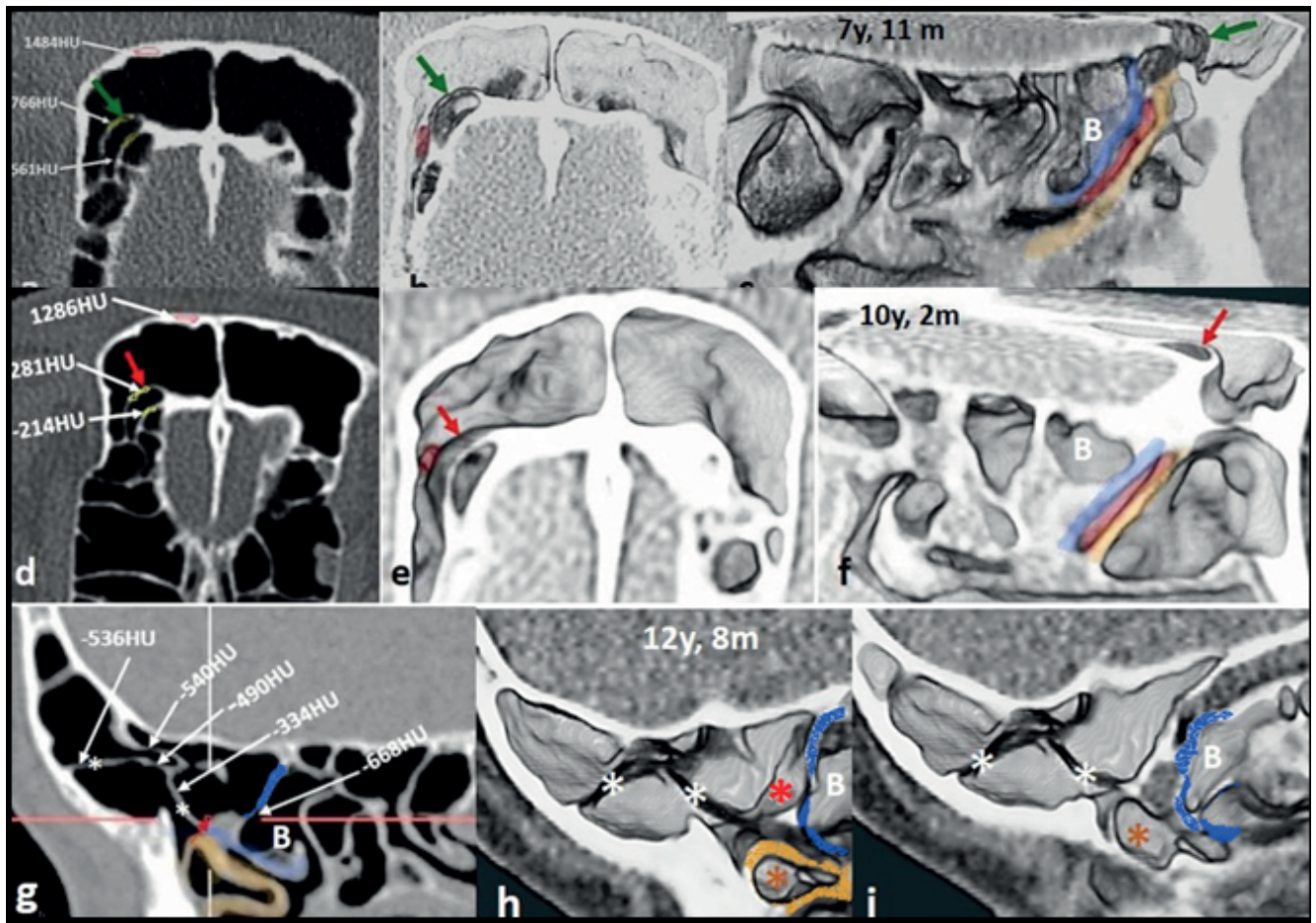


Figure 7: The development of a fronto-ethmoidal space over a 27 months interval, & a fronto-ethmoidal/frontal bulla space in a 12 year-eight month old patient.

a.-c. A 7 year, 11 month old patient with standard axial CT image fig. (a.), 3D axial image viewed from above fig. (b.), and 3D sagittal view of the fronto-ethmoidal anatomy fig. (c), which reveal the ethmoidal extension into the FS (green arrows). Note the dark membranous outline of the ethmoid space extension (green arrows) into the FS. The expanding lamellae have a density of -766HU/-561HU, with the frontal calvarium having a density of 1484HU. Uncinate lamella (gold), EB (blue), and EI (red).

d.-f. Same patient at 10 years, 2 months, with standard axial CT image fig. (d.), 3D axial image viewed from above fig. (e.), and 3D sagittal view of the fronto-ethmoidal anatomy fig. (f.). The images reveal the ethmoid expansion into the FS (red arrows). Note that the “cut” surface density of the expanding lamella, has a central bony density in figs. (e., f.), and corresponding densities in g. are -281HU/-214HU, while calvarial bone has a density of 1286. Comparing the appearance, as well as the density changes, at both ages indicates that the dark lamella is transitioning into a cartilaginous/bony structure.

g. Standard sagittal CT image focusing on the right AES/FS (center outlined by the “cross hair” lines, and small red arrow), display the lamella tissue densities in Hounsfield Units (HU). The specific area of interest corresponds with figs. (h.,i) 3D sagittal images. Bone density is more or less 1200HU; cartilage is more or less 350HU; soft tissue is at or above 0HU; air is -1,000 HU and the faint dark membranous outline, described above, range between -330HU and -670HU.

h., i. 3D Sagittal images focused on the AES and FS in a 12 yr, 8 month old patient, reveal the “dark lamella like” membranous structure (white asterisks) noted to arise from the junction of the bulla lamella (blue outline) and uncinate lamella (gold outline). Note that, posteriorly, the dark lamella is fused with a cartilaginous structure (red asterisk), which adheres to the bulla lamella. In the FS, the irregular outline of the “dark lamella” appears to initiate the creation of a “bullous space” within the FS and has the characteristics of an evolving fronto-ethmoidal space or a frontal bulla.

bular groove⁽⁸⁾. Our observations on 3DCTSI reveals that the FR is an extension of the EI. However, both the FR and MM can penetrate the cancellous bone of the frontal bone individu-

ally, or conjointly if the precursor of the FS, is first, the FR, thus providing the MM the space to penetrate into the medial floor of the FS.



Figure 8. The Frontal Sinus & Septum's appearance at various ages of development.

3D axial images viewed from above, except for two 3D coronal images, so indicated on the specific images. The images are at various ages of FS development and demonstrate the variability in FS and inter-frontal sinus septal development. Note that, at age three years and two months, the FS is absent. FS expansion is readily observed after the age of five years, four months. At five years and six months in this patient there is an asymmetry in the FS expansion, with a "thin" paramedian frontal septum created by the "collocation"/fusion of the medial boundaries of the expanding right and left FS. ". The asymmetry of the FS and the unilateral expansile nature of a single sinus (at 10 years, three months) is shown. Similarly, in a patient at 12 years, three months, the anterior coronal image may lead one to consider the presence of an inter-frontal sinus septal cell, however, the 3D axial images reveal that bony ridges in the floor of the FS adhere to the frontal septum, creating a distorted frontal sinus, which gives the appearance of an IFSSC. Similar bony ridges in the outline of the "excavated" frontal bone affect the frontal septum in the patient at 16 years, one month. Frontal sinus septum (+).

Since human pediatric sinuses cannot be examined systematically, non-human primates, offer tractable models of sinus development⁽³³⁻³⁷⁾. Previously, Smith et al. found that primates developing maxillary and frontal sinuses have a more fragmented lateral nasal capsule, than primates without the frontal and maxillary sinuses. At earlier stages of development, the lateral wall of the cartilaginous nasal capsule is more complete. This suggests that cartilage may be considered to be the "gate-keeper" that determines the timing of secondary pneumatization⁽³⁵⁾. Histological studies of tamarin monkeys (e.g., *Saguinus* spp) reveal details which are currently precluded from radiological display. Notably, cartilage breakdown by resorption (e.g., evidence of chondroclasts) or other mechanisms is seen prior to pneumatic expansion of sinuses^(37,38).

Based on these observations, we hypothesize that the human fronto-ethmoid sinus system develops in a similar manner, following localized cartilage resorption or breakdown. Further work with animal models might elucidate radiological properties of cartilage, which is known to undergo tissue-level changes as the nasal cavity develops⁽³⁸⁾, to enhance our ability to track human sinus development.

Bone forms by direct or indirect routes. In "indirect" forms of ossification, bone replaces an existing tissue, such as cartilage⁽³⁹⁾. Intramembranous bone forms directly within mesenchymal tissue in association with a "membrane" (i.e., a collagenous fascia). Mesenchymal cells differentiate into bone-producing cells (osteoblasts) at these sites, producing bones of the superficial facial skeleton, clavicle, and distal phalangeal tips.

Our observation regarding the 'dark membranes' is discussed in this context. Pertinent to the present study is the fact that additional elaboration of bones occurs even after bones are first formed. Generally, this bone is produced on the external surfaces of existing bone, and the process is termed "appositional growth." Bone is produced by osteoblasts that migrate to the bone's surface from the periosteum, and it is laid down on external surfaces; this is considered analogous to intramembranous bone formation (Figure 6)⁽⁴⁰⁾. Such bone has long been acknowledged to make endochondral bones more elaborate after they are ossified, and the new bone is known to follow membranes such as fontanelles of the skull⁽⁴¹⁾. Similarly, we suggest that the bony lamellae that separate ethmoid air cells originate from existing ethmoid surface and invade existing membranous

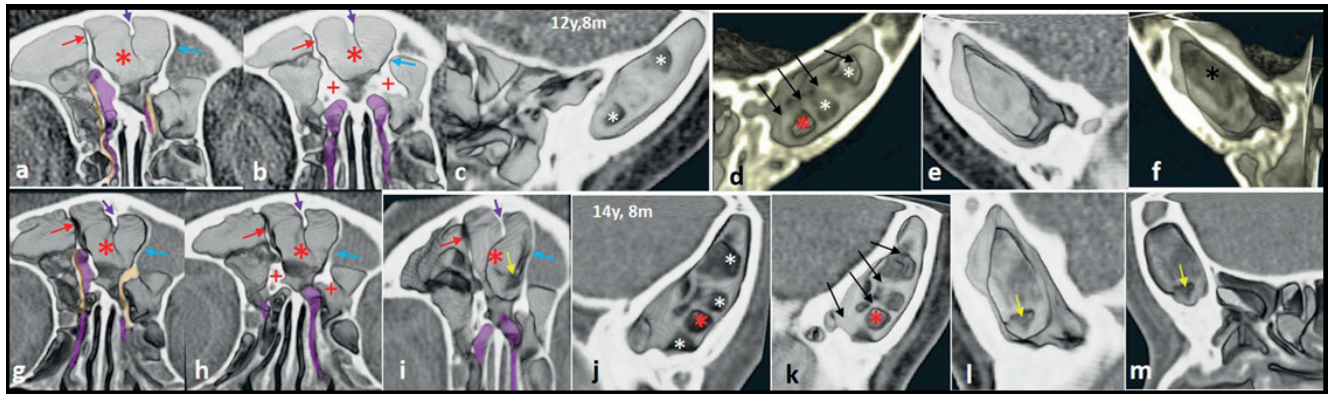


Figure 9. Inter-Frontal Sinus Septal Cell (IFSSC): development over a course of two years.

a.-f. 3D images of a 12-year, 8 month old patient. 3D coronal images (a., b., with b. being Inferior to a.), reveal that the antero-superior extension of the MM bilaterally (purple outline), is accompanied by the anterosuperior extension of the UL laterally and the MT medially, which fuse anterior to the MM termination. The fusion of the UP and MT continues forward to the anterior frontal sinus wall, as a "common lamella", creating a left paracentral septation (red arrow). A right para-central septation is created by the extension of the UL (gold outline) (fig. a.). Note in fig. (b.) the two posterior para-central lamellae adhere at a bony groove arising from the antero-inferior FS (red +). In both (figs. a., b.), an anterior bony ridge (purple arrow) is noted in the floor of the central space, i.e. the IFSSC (red asterisk).

Fig. (c.) 3D sagittal image, standard windowing and fig. (d.), bony windowing of the medial surface of the left paracentral lamella. Figs. (e., f.), similar windowing of the medial right paracentral lamella. The images of the left paracentral lamella reveal "dark membranous" outlines covering apparent openings in the bony ridges, created by bony ridges arising from the anterior surface of the frontal bone, extending posteriorly to the posterior FS wall. On the right side the paracentral lamella appears to be intact, however, a dark shadow is present on the bony windowed image (black asterisk). g.-m. 3D images of same patient at 14-years, 8 months, with similar 3D coronal images (g.-i.) and sagittal 3D images (j.-l.) of the paracentral lamellae. In addition, an obliqued 3D coronal image (fig. i.) was added to better display the central bony ridge (purple arrow), and show its prominence as it adheres infero-posteriorly to the bony ridge. It also adheres to the infero-posterior right paracentral lamella. The 3D sagittal images of the paracentral lamellae medial appearance are with standard windowing in images (k., i.), shown with increased brightness. Note the increased "transparency" of the membrane outlined by the red asterisk in both ages, and the potential of a "breakthrough" which would provide communication with the ipsilateral FS. The "dark shadow" (yellow arrow) may provide a similar process on the right side.

septa (i.e., the dark membranes) (Figures 4-6).

As early as the first month of life well defined and irregular dark outlines are noted in the medial LP which with increasing age (1-4 years of age) become enclosed by a dark membranous structure. Similar dark outlines are also present along the edge of bony grooves also which arise from the medial LP, and from which, parallel dark membranous sheath extend medially adhering to fragmented lamella created in the breakdown stage.

The appearance of the dark membrane on the 2D CT imaging is limited since it is being displayed on a single 0.7mm thin slice/image and therefore has a very weak CT signal. However, with 3D volume-rendering, the volumetric display of the region of interest, indicate that the density of the dark membrane most likely represents a precursor to cartilage and bone formation (Figures 4-6, 8).

The increase in density of the lamina propria is caused by bony islets expanding in the lamina propria from peripheral bone (Figure 6). The penetration of bony islets may be compacted into the lamina propria creating a homogenous appearance (Figures 3-6), or may appear in a tattered configuration, an early phase of

bony islets adherence within the lamina propria (Figure 5). The presence of the dark membrane is easily noticed on the 3D reconstructed images, and does not represent shadows. It is made possible by the 3DCTSI combining a block of several 0.7mm CT images. Given the information available from the studies of non-human mammals it is our belief that the dark membrane is comprised of 2 parallel mucosal epithelium layers "sandwiching" a core of lamina propria between them (Figures 4-7), "appositional bony growth" and when evaluated with HU density measures reveals a transition from soft tissue to bone (Figure 7).

Our observations also allow an extended discussion about the development of the frontal sinus with its structural components:

- The frontal sinus drainage has been the topic of recent publications⁽⁴²⁻⁴⁴⁾. On 3DCTSI, the frontal sinus drainage pathway is primarily accomplished through the FR and subsequently the EI, and/or through the MM. Less frequently the FR has a direct communication with the ISEUP or the Supra Bullar Recess space to then communicate with the EI and/or the MM⁽³¹⁾.
- The frontal sinus septum is a medial/paramedial complete separation within the frontal sinus arising from the bonding of the medial surfaces of the expanding lateral frontal sinus cavities

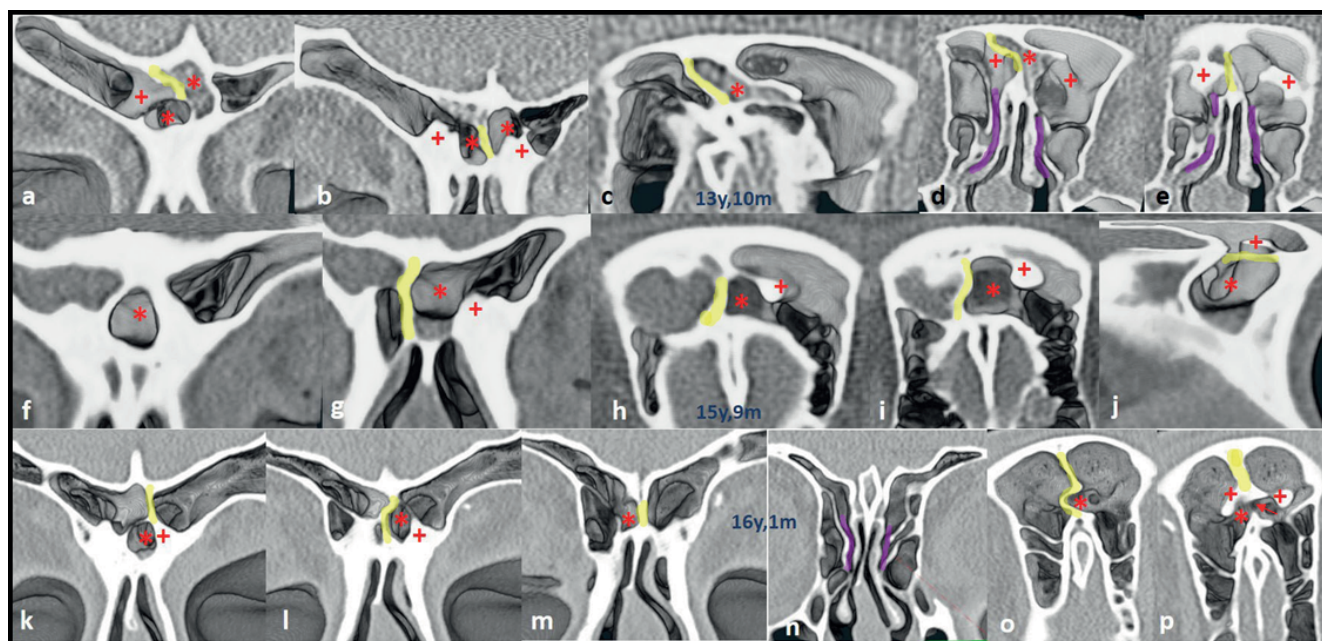


Figure 10. Frontal Inter-Sinus Septal Cell "mimics".

a.-e. 3D images from a 13 year, 10 months old patient: fig. (a.) anterior to fig. (b.) are coronal images, which reveal two paracentral spaces (red asterisks) adjacent to the FS (yellow). In fig. (b.) note that both apparent spaces open into the posterior frontal sinuses. Note throughout the remaining images: fig. (c), 3D axial image viewed from above, and figs. (d., e.) 3D coronal images viewed from posteriorly, all reveal that both "apparent spaces" on the axial images are the result of bony ridges arising from the antero-inferior margin of the frontal bone. The MM (purple outline) is in communication with the FS bilaterally.

f.-j. 3D axial image from a 15 year, 9 months old fig. (f.) reveals an apparent central space (red asterisk), which in fig. (g.), just posterior to fig. (f.) is to the right of the FSS (yellow) and opens to communicate with the right FS. In figs. (h., j), 3D coronal images, and fig. (j.) 3D sagittal image viewed from left medially, note the bony ridge (red +) arising from the antero-inferior FS and is the creator of the "apparent" central space.

k.-p. 3D axial images from a 16 year, 1 month old patient, viewed sequentially from anterior to posterior, reveal two "apparent" spaces adherent to the FSS (yellow) on each side, both opening into the posterior FS. Figure (n), is a 3D coronal image showing the communication between the MM (purple) and the FS on each side. Figs. (o., p.), 3D axial images viewed from above, reveal the "undulating" course of the FSS, and its communication with bilateral bony ridges which have a "wishbone" configuration, previously described. Note a break in the continuity of the FSS affording communication between the bilateral FSs (red arrow).

which steadily replace the midline cancellous frontal bone (Figure 8b). This entity is not to be confused with IFSSC (discussed below) (Figure 9), and the incomplete septations resulting from bony grooves arising from the antero-inferior surfaces of the frontal sinuses (Figure 10).

- The Inter-Frontal Septal Cell (IFSSC): the fusion of the antero-superior middle turbinate and UP anterior to the enclosed MM within the medial FS creates the "paracentral lamella" which extends anteriorly as it also partially fuses with bony grooves along the antero-inferior FS. The fusion with the bony grooves may be incomplete creating opening(s) in the lamella (Figure 9). The opening(s) may be sealed by an evolving "dark membrane", which with age may convert to bone, creating a solid paracentral septation. If the opening is not sealed, a communication remains between the FS and the midline space. Irrespective of the communication afforded by openings in the paramedial

septation(s) the midline space is noted to communicate with the MM bilaterally (Figures 9, 10). To date the origin of the IFSSC has been considered to be the result of a diverticular process^(17, 18). However, 3DCTSI reveals that the IFSSC is created by a developmental process with potential openings within the paracentral septations as these fuses with bony ridges within the outline of the FS. Thus, the central space will communicate with the peripheral FS (es) as well as the MM bilaterally and therefore the central space cannot be the result of a diverticular process⁽⁴⁵⁾.

Conclusions

Since the introduction of FESS in the 1980s, we have witnessed numerous advances in surgical techniques, strategies and instrumentation accompanied by advances in imaging. Each advance in imaging from plain X-ray imaging to X-ray polytomography to single plane CT imaging to CT MPR improved the display and understanding of the nasal cavity and paranasal sinus anatomy.

The ability to decrease the CT slice thickness from 2mm (late 1980s) to 0.7 to 0.1mm (recently) significantly improves the 3D CT volumetric display with a markedly improved perceptive understanding of this regional anatomy.

Several publications have described the adult anatomy of the nasal cavity and paranasal sinuses; however, few have dealt with the detailed development of the pediatric ethmoid and frontal sinuses. With this presentation, our objective was to begin a discussion of the Ethmoid and Frontal Sinuses' development, by demonstration of the intuitiveness shown on 3DCTSI. The presentation of three stages of Ethmoid sinus development, the role of the dark lamella in transitioning from soft tissue to bone and the creation of the final ES spatial contours, as well as the role of the ES in creation of the FS and its compartmentalization, is meant to provide a platform for future discussions. It is also intended to provide a better understanding of the complexity and variability of this anatomic region, and potentially, facilitate the planning and performance of minimally invasive surgical procedures.

Authorship contribution

SJZ, FAK, SM, and WH contributed to the writing and edited the anatomic detail; MS assisted in creating the needed images.

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The 3DCTSI evaluation of the nasal cavity and paranasal sinuses began in 2017 with Heinz Stammberger's assistance. His passing in 2019 left a large void in our team. His enthusiasm and pursuit for continued improvement in the display and understanding of the nasal anatomy continued to be an inspiration in our work as it is carried forward. We miss him as a friend and teacher.

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Conflict of interest

W. Hosemann is a consultant for Karl Storz. F. Kuhn, S. Marquez, M. Solaiyappan, and S. Zinreich have no conflicts of interest.

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