The Sutures of the Skull - Anatomy, Embryology, Imaging, and Surgery

CHAPTER 11: A brief introduction on the biomechanics of craniofacial sutures

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Abstract

The biomechanical studies on the craniofacial sutures can be classified to three groups, to understand: (1) the inherent mechanical properties of the sutures; (2) role and function of the sutures (using in vivo and in silico techniques) and (3) how sutures respond to mechanical loads (using in vitro or in vivo experiments). The aim of this chapter was to provide a short overview of the biomechanics of the sutures under the aforementioned categories. This chapter can be consider as an introduction to the biomechanics of the sutures and readers are encouraged to read throught the papers reviewed here.

Keywords
suture, skull, biomechanics, craniosynostosis, bone, craniofacial system

11.1 Introduction

Sutures are composites of mesenchymal cells that during development differentiate and deposit extracellular matrix consisting primarily of collagens as well as various bone-related proteins and proteoglycans [1,2]. Sutures are an integral part of the craniofacial system that together with the synchondroses modulate the growth and development of the craniofacial system [3,4] while their premature fusion leads a clinical condition called craniosynostosis [5,6].

During the development, sutures accommodate the radial expansion of the brain [7,8]. By the time the brain has reached its maximum size, visible gaps at the sutures have reduced to micro/nanometer gaps where sutures have differentiated to bone [9]. A few of the sutures fuse but a large number of them remain open during adulthood with different morphologies, butted, overlapping and with varying degrees of interdigitations [10-12]. During the adulthood, they contribute to a uniform distribution of the mechanical loads applied to the craniofacial system and act as shock absorbers [13-15]. The mechanical loads that sutures experience arise from e.g. the growth of internal organs in the craniofacial system such as brain and eye; from daily activities such as biting; or from sudden impact from external objects [16].

A wide range of techniques such as tensile testing, nanoindentation, strain gauging and finite element methods have been used to understand the biomechanics of the sutures. These studies can be classified to three groups, to understand: (1) the inherent mechanical properties of the sutures; (2) role and function of the sutures (using in vivo and in silico techniques) and (3) how sutures respond to mechanical loads (using in vitro or in vivo experiments). Under each category, there is a wealth of literature.

The aim of this chapter was to provide a short overview of the biomechanics of the craniofacial sutures under the aforementioned categories. The goal of this chapter was not to offer a critical review of past studies nor to summaries the whole literature. Instead, the goal was to inform the reader of the key ongoing research areas, provide a brief overview of the methodologies used and highlight the key studies to the best of our knowledge. Readers are referred to studies cited here and other reviews on the mechanobiology of sutures [17-20].

11.2 Inherent mechanical properties of the sutures

Tensile/compression testing, three/four-point bending and indentation are the most commonly used techniques to characterise the mechanical properties of the sutures on a wide range of species (see the review of such studies in human by Savoldi et al. [21]). In brief, these techniques characterise the load-displacement of the sutures under a specific loading rate and based on this data estimate parameters such as the elastic modulus, yield and ultimate stress. There are a number of key factors in such studies. These can be classified into the biological related factors such as species, anatomical region and age or testing related factors such as loading approach, loading rate, and indentation tip.

It is widely accepted that sutures are viscoelastic materials where their mechanical property are nonlinear and is influenced by the loading rate and its duration [16,22]. Nonetheless, a few studies have characterised the viscoelastic properties of the sutures. Studies of Tanaka et al. [22], Margulies and Thibault [23] and Popowics and Herring [24] are some the classical examples that reported Elastic modulus of the sutures under different loading rates. At the same time, there is a good body of literature that has quantified the elastic modulus of the sutures using a specific set of parameters in comparative studies. Table 1 summarises some of the key studies to the best of our knowledge. It is clear that elastic modulus that has been reported for the sutures varies considerably. This can be due to the aforementioned factors involved in these studies. Also given that tissue differentiation is present across the sutures, at least during the development, it can be expected that the elastic modulus of the suture can vary across the sutures. In this respect, indentation is a powerful tool to characterise such variation across the cross-section of the sutures. Overall it seems that the elastic modulus of the sutures is in the range of low MPa (1-30MPa – see Table 1).

11.3 Role and function of the sutures

A range of techniques such as in vivo, ex vivo strain gauging, and in silico computational methods have been used to quantify the level of loading across the craniofacial system and sutures. Given that sutures are mainly loaded during biting, themajority of these studies have focused on biting and its associated muscles and soft tissues. Clearly in vivo studies are the “gold standard” to quantify the loading level across the sutures. Nonetheless, the computational models are powerful tools to answer a variety of “what if” questions and ex vivo studies are invaluable to validate the in silico studies.

In vivo studies have mainly placed strain gauges across the skull and recorded strain across the bones and sutures during various biting scenarios. To the best of our knowledge, fewer studies have specifically used this technique to measure the strain across the sutures. There are several studies e.g. in fish [36], lizards [37,38], rat [39], pig [40-43] and macaque [44-45] where in vivo strain across a range of sutures have been measured. These studies broadly highlight that there is a correlation between the morphology of the sutures and the predominant loading that they undertake with high interdigitate sutures being mainly loaded under compression, the overlapping sutures under shear and butted sutures under tension.

In silico studies have mainly used finite element (FE) method (see following textbooks on this method [46, 47]). This computational technique enables us to carry out a structural analysis that can predict the deformation of the skull under a particular loading regime (see the reviews by Rayfield

[48] and Prado et al. [49]). It is a powerful technique where a variety of scenarios can be modelled and a wide range of questions can be asked and answered in a cost-effective manner. This method requires various input parameters i.e. morphology of the skull, inherent properties of various constituents of the skull e.g. bones and sutures and loading applied to the skull.

FE models have been widely used in the past 30 years to understand the role and function of sutures in a range of species with a range of evolutionary, functional, developmental and clinical questions (see Table 2). Perhaps one of the early studies with evolutionary and functional questions that used FE method to model sutures is the study of Rayfield et al. [50], a case study on a dinosaur. The same approach was then adopted by many others to study roles of sutures in e.g. lizards [15, 51, 52], Sphenodon [53], macaque [54-55], pig [56] and recently in amphibian [57]. Studies using the FE method to model the development of the craniofacial system (i.e. modelling the sutures) seem to be far more limited. A few recent studies have recently used this technique to model the development of calvaria in mouse [58-61] and human [62-65]. Similarly, a few studies have used FE method to inform clinical management of conditions associated with craniofacial sutures such as cleft lip/palate [e.g. 66-68] and craniosynostosis [e.g. 69-73 and see the review by Malde et al. [74]).

Regardless of the application of the FE method, the validation of these models is crucial to build confidence in their outcomes. Hence, a wide range of validation studies have been carried out by comparing the FE results versus in/ex vivo strain gauging or recently using laser speckle interferometry. Perhaps some of the key studies in this respect are studies Kupczik et al. [75] and Wang et al., [45] in macaques; Bright and Groning [76] in pig; Cuff et al. [77] in ostrich. Overall, FE studies have already shown that sutures play an important role in distributing the strain across the skull more uniformly and have clearly shown the potentials of this method to advance the treatment of various clinical conditions.

11.4 Sutures response to the mechanical loads

In vivo and in vitro experimental loading set ups have been developed and used to test the response of sutures to controlled loading regimes. The loading has been either quasi-static (compressive or tensile) or dynamic (compressive or tensile). Perhaps the classic in vivo example of applying forces to the sutures is cranial deformation. This has been practiced by various human groups in e.g. North and South American Indians, Pacific Islander and various European stocks resulting in e.g. circumferential or anteroposterior deformed crania [78, 79]. While the level of loading that has been applied in these cases is unknown, the skull is clearly deformed but interestingly various sutural morphologies do not seem to be affected.

A large body of literature has carried out various in vitro experiments where a section of the skull including the sutures have been placed and loaded in a dish. These controlled experiments have enabled us to study the cellular and morphological changes in the sutures with their main limitations being their in vitro nature i.e. lacking the blood supply, surrounding anatomical structures and alteration in the overall mechanics of the tissues. One of the early studies that used such an approach was the study of Meikle et al. [80] on a rabbit model followed by several other groups [81-85]. See the review by Alaqeel et al. [86] for a detailed summary of in vitro loading experiment studies on the sutures (and also in vivo studies). They summarised the various changes in e.g. protein level, growth factor expression, and extracellular matrix of sutures due to the mechanical forces.

A relatively large body of literature has also carried out in vivo studies where various sutures have been loaded under different loading regimes and durations. Table 3 provides a summary of the key in vivo experiments that have been carried out to the best of our knowledge. These studies together with the in vitro studies highlight that external tension across the sutures up-regulate sutural cell proliferation, increasing the number of cells and their macroscopic width. The quasi-static tensile force seems to have a limited effect [87] while dynamic loading seems to have a larger and perhaps a longer lasting effect. A Study from Kopher and Mao [88,89] highlighted that both tensile and compressive cyclic loading may also enhance maintenance of the sutures. Nonetheless, our understanding of the impact of various parameters in such studies (loading duration, frequency etc.) are still limited and largely based on pioneering studies of Mao's team.

11.5 Discussion

A short summary of the literature on the biomechanics of the sutures was provided here. There is no doubt that there is a wider literature that is not covered here and the readers are encouraged to further research. For example, there are a number of studies that have focused on modelling and understanding the sutural morphologies [105-107] or there is a wider literature on using FE method in addressing various clinical conditions associated with the craniofacial system. Overall, we feel that this chapter can be a good initial read for those beginning to explore the biomechanics of sutures, pointing them to the relevant literature.

Considering the topics covered here, the material testing experiments to date have significantly advanced our understanding of the inherent mechanical properties of the sutures. Perhaps further studies can use this technique to quantify the changes in the mechanical properties of the sutures during the development or in various craniofacial abnormalities. Similarly, computational and in vivo experiments can be further implemented to advance our understanding of various craniofacial conditions such as craniosynostosis. Indeed, combining various techniques such as geometric morphometric, finite element, machine learning and experimental techniques can be a powerful approach to address various non-clinical questions [see e.g. 108]. External loading studies of the sutures have so far mainly focused on the normal sutures, applying same methodologies to various animal models of craniofacial conditions [109-110] is another key avenue of research that requires further attention. This can potentially lead to the development of novel technologies for the treatment of conditions such as craniosynostosis.

There is no doubt that the whole field of suture mechanobiology has had an immense progress in the last 30 years, advancing our fundamental understanding of this topic. We have already seen several examples that have found their way from basic science research to clinical practice. For example, spring-assisted cranioplasty is nowadays becoming a popular treatment option for the management of sagittal craniosynostosis [see e.g. 111] with early studies in the 1970s applying the same concept to various animal models. There are indeed large bodies of ongoing research e.g. in the fields of tissue engineering and gene therapies [e.g. 112-114] that can potentially revolutionize the treatment of craniofacial conditions in years to come.

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Table 1: A summary of some of the key studies characterising the elastic modulus (E) of the sutures. Note C= compression; T= tension; NC= not clear to us.

Author	Animal	Age	Suture	E (MPa)	Testing Method
Jaslow [25]	goat	2-4years	internasal and coronal	10-35* & 120-240*	three-point bending
Thibault et al. [26]	human	3 months	coronal	189~	tension
Margulies and Thibault [23]	pig	2-3 days	coronal	194.2 ± 42.5	three-point bending
McLaughlin et al. [27]	rat	7 days	sagittal, coronal & posterior frontal	13, 14 & 2.3	tension
Tanaka et al. [22]	rat	4 weeks	sagittal	4.5±1.8**	tension
Radhakrishnan and Mao [28]	rabbit	8 weeks	pre-maxillomaxillar, nasofrontal & zygomaticotemporal	1.5 ± 0.2, 1.2± 0.2 & 1.2±0.2	atomic force microscopy
Henderson et al. [29]	rat	2-60 days	sagittal	4-80^	three-point bending
Coats and Margulies [30]	human	21 weeks gestation-12 month	coronal	3.8-16.2	tension
Grau et al. [31]	human	9.1±2.8 months	synostosed metopic & synostosed sagittal	0.5 ± 0.1 & 0.7 ± 0.2	nano-indentation
Popowics et al. [24]	pig	3-6 weeks & 5-6 months	nasofrontal	68±32 (C); 43±16 (T) & 115±45 (C); 70±33 (T) “	compression (C) & tension (T)
Davis et al. [32]	human	6 years	NC	1100±530	four-point bending
Wang et al. [33]	human	1.5±0.5 years	coronal & sagittal	354.8 ± 44.9 & 408.1 ± 59.1	three-point bending
Rahmoun et al. [34]	human	average of 88 years	coronal	2038.4 ± 923.6	three-point bending
Moazen et al. [35]	mouse	10-20 days	sagittal, coronal & posterior frontal	20±12, 29±23 & 34±33	nano-indentation

*Bending strength was reported in this study; ~ mean stiffness was reported in N/mm;^ average value of 22MPa calculated based on suture thickness; “at a higher loading rate of 0.02mm/s;**relaxed moduli was estimated following a series of loading-unloading detailed in the paper.

Table 2: Short summary of key finite element studies modelling the cranial sutures.

Author	Animal	
Rayfield et al. [50]	dinosaur	evolutionary focus
Kupczik et al. [75]	macaque	
Wang et al. [45, 54, 55]	macaque	
Moazen et al, [15, 51]	lizard	
Bright and Groning, [76]	pig	
Bright [56]	pig	
Curtis et al. [53]	sphenodon	
Cuff et al. [77]	ostrich	
Jones et al. [52]	lizard	
Gruntmejer et al. [57]	amphibian	
Jin et al. [62]	human	developmental focus
Lee et al. [58,59]~	mouse	
Burgos-Florez et al. [63]	human	
Libby et al. [64]	human	
Weickenmeier et al. [65]	human	
Marghoub et al. [60,61]	mouse	
Pan et al. [66]	human	clinical focus
Nagasao et al. [69,70]	human	
Chen et al. [67,68]	human	
Borghi et al. [71]	human	
Malde et al. [72]	human	
Bozkurt et al. [73]	human	

~a finite volume study

Table 3: A summary of key in vivo studies investigating the effect of external loads on the craniofacial sutures. See also studies of Wang and Mao (on rabbit cranial base – [90]) and Tang et al. (on rat cranial base – [91]). NK=not known to us; Q-static=quasi-static.

Author	Animal	Age	Suture	Level of loading	Duration	Q-static or dynamic
Cleall et al. [92]	macaque	P90-120	midpalatal	4mm expansion achieved in 2 weeks then 2mm at 4 weeks interval up to 12 weeks	several intervals from 2 -36 weeks	Q-static tension
Elder and Tuenge [93]	macaque	NK	several sutures	700 Gm at 40degree angle to the occlusal plane was applied via a frame to the maxilla	57-72 days	Q-static tension
Ten Cate et al. [94]	rat	NK - adults	sagittal	2mm deflection was induced in a wire frame that was placed across the sagittal suture	various intervals from 2h to 42days	Q-static tension
Jackson et al. [95]	macaque	P1200-P1440	several sutures	300 Gm per side parallel to the occlusal plane was applied via a frame to the maxilla	63-114 days	Q-static tension
Southard and Forbes [96]	rat	P53-58	interpremaxillary	50 to 75 g , 150 to 175 g and 250 to 300 g was applied via a helical spring (made from stainless steel) across the maxillary incisors	12 hours; 1,2 and 4 days	Q-static tension
Anton et al. [78]	human	unknown	several sutures	unknown – intentional head deformity	unknown	Q-static
Losken et al. [97]	rabbit	P10	coronal	A total 3.97mm distraction was applied to the coronal suture over 42 days	2 times per week for 6 weeks - P28-P70	Q-static
Bradley et al. [98]	lamb	85-95 days gestation	coronal	1mm compression plate was placed across the mid portion of the coronal suture	28 and 56 days	Q-static compression
Tanaka et al. [99]	rat	P28	sagittal	65g expansion was applied across the sagittal suture	for 15, 30 and 50h	Q-static tension
Kopher and Mao [100] and Kopher et al., [88]	rabbit	P42	premaxillomaxillary , nasofrontal	5 N (compressive) applied to the maxillary incisors at 0 Hz & 1 Hz (sine & square wave)	10 min/day for 12 days	Q-static and dynamic
Mao et al. [89]	rabbit	P42	premaxillomaxillary	2N (tensile) applied to the maxillary incisors 0 Hz, 0.2 Hz & 1 Hz	10 min/day for 12 days	Q-static and dynamic
Vij and Mao [101]	rat	P17, P23, P32	Premaxillomaxillary , nasofrontal	0.3N (compressive) applied to the maxilla at 4Hz	20min/day for 5 days	dynamic
Peptan et al. [102]	rabbit	P42	Premaxillomaxillary , nasofrontal	1N (tensile and compressive) applied to the maxillary incisors at 8 Hz & (sine wave)	20min/day for 12 days	dynamic

Han et al. [103]	macaque	P960	several sutures	3N was applied via cast class III magnetic twin-block appliance to the upper	for 45 and 90 days	static
Takeshita et al. [87]	mouse	P42	sagittal	0.2N was applied to the sagittal suture by bending and placing a 0.3mm diameter nickel-titanium wire	For 28 days	static
Soh et al. [104]	pig	P90	nasofrontal	800-1000micros strain (tensile) was applied to the nasofrontal at 2-3 Hz	30min/day for 5 days	dynamic