Chapter 11
A Brief Introduction to the Biomechanics of Craniofacial Sutures

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11.1 Introduction

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

During 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 diminished to micro/nanometer gaps where they have differentiated to bone [9]. A few sutures fuse, but many remain open during adulthood with different morphologies: abutted, overlapping, or to various degrees interdigitated [10–12]. During adulthood, they help to ensure 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 by external objects [16].

A wide range of techniques such as tensile testing, nanoindentation, strain gauging and finite element methods have been used to elucidate the biomechanics of the sutures. These studies can be classified in three groups: to understand (1) the inherent mechanical properties of the sutures; (2) the 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). There is a wealth of literature under each category.

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The aim of this chapter is to provide a short overview of the biomechanics of the craniofacial sutures under the aforementioned categories. The goal is not to offer a critical review of past studies or to summarize the entire literature. Rather, the objective is to inform the reader about key ongoing research areas, provide a brief overview of the methods used, and highlight the key studies to the best of our knowledge. Readers are referred to the 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 common techniques used to characterize the mechanical properties of sutures in a wide range of species (see the review of such studies on humans by Savoldi et al. [21]). In brief, these techniques characterize the load-displacement of the sutures under a specific loading rate, and on the basis of those data estimate parameters such as the elastic modulus, yield and ultimate stress. There are several key factors in such studies: biologically related factors such as species, anatomical region and age, and testing-related factors such as loading approach, loading rate, and indentation tip.

It is widely accepted that sutures are viscoelastic materials, the mechanical properties of which are nonlinear and are influenced by the rate and duration of loading [16, 22]. Nonetheless, a few studies have characterized the viscoelastic properties of sutures. Classical work by Tanaka et al. [22], Margulies and Thibault [23] and Popowics and Herring [24] reported the elastic moduli of sutures under different loading rates. At the same time, a good body of literature has quantified the elastic moduli using a specific set of parameters in comparative studies. Table 11.1 summarizes some of the key studies to the best of our knowledge. It is clear that there is considerable variation in the reported values of the elastic moduli, probably because of the aforementioned factors. Also, given that the sutures are undergoing tissue differentiation , at least during development, it can be expected that the elastic modulus will vary across a suture. Indentation is a powerful tool for characterizing such variation. Overall, it seems that the elastic moduli of the sutures are in the range 1–30 Mpa, which are quite low values (Table 11.1).

11.3 Role and Function of the Sutures

A range of techniques such as in vivo and 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,

Table 11.1 Some key studies characterizing the elastic moduli (E) of sutures

Author	Animal	Age range	Clinical focus	Evolutionary focus	Developmental focus
Jaslow [25]	Goat	2–4 years	Internasal and coronal	10–35[a] & 120–240[a]	Three-point bending
Thibault et al. [26]	Human	3 months	Coronal	189[b]	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[c]	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[d]	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 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

[a] Bending strength was reported in this study
[b] Mean stiffness was reported in N/mm
[c] Relaxed modulus was estimated following a series of loading-unloading detailed in the paper
[d] Average value of 22 MPa calculated based on suture thickness; “at a higher loading rate of 0.02 mm/s
Note: C: compression; T: tension; NC: not clear to us.

most of these studies have focused on biting and its associated muscles and soft tissues. Clearly, in vivo studies are the “gold standard” for quantifying the loading level across the sutures. Nonetheless, computational models are powerful tools for answering various “what if?” questions, and ex vivo studies are invaluable for validating 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 used this technique to measure strain specifically across the sutures, though several studies on e.g., fish [36], lizards [37, 38], rats [39], pigs [40–43] and macaques [44, 45] have measured in vivo strain across a range of sutures. These studies broadly highlight a correlation between the morphology of the sutures and the predominant loading they experience, highly interdigitated sutures being mainly loaded under compression, overlapping sutures under shear and abutted sutures under tension.

In silico studies have mainly used the 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 by which a variety of scenarios can be modeled and a wide range of questions can be asked and answered cost-effectively. This method requires various input parameters, i.e. the morphology of the skull, the inherent properties of its various constituents e.g., bones and sutures, and the loading applied to it.

FE models have been widely used over the past 30 years to elucidate the role and function of sutures in a range of species and to address a range of evolutionary, functional, developmental and clinical questions (see Table 11.2). Perhaps one of the earliest studies exploring evolutionary and functional questions and using FE to model sutures was by Rayfield et al. [50], a case study of a dinosaur. The same approach was then adopted by many others to study the roles of sutures in e.g., lizards [15, 51, 52], Sphenodon [53], macaques [54, 55], pigs [56], and recently amphibians [57]. Far fewer studies seem to have used the FE method to model the development of the craniofacial system (i.e., modeling the sutures). A few recent ones have used this technique to model the development of calvaria in mice [58–61] and humans [62–65]. A few others have used FE 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, validation of these models is crucial for building confidence in their outcomes. Hence, a wide range of validation studies have been carried out by comparing the FE results with in/ex vivo strain gauging, and recently with laser speckle interferometry. Perhaps some of the key studies in this respect are Kupczik et al. [75] and Wang et al., [45] on macaques; Bright and Groning [76] on pigs; and Cuff et al. [77] on ostriches. Overall, FE studies have demonstrated the importance of sutures in distributing strain across the skull more uniformly and have clearly shown the potential of this method to advance treatments of various clinical conditions.

Table 11.2 Short summary of key finite element studiesmodelling the cranial sutures

Author	Animal
Rayfield et al. [50]	Dinosaur
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
Lee et al. [58, 59][a]	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
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] A finite volume study

11.4 Response of Sutures to Mechanical Loads

In vivo and in vitro experimental loading setups have been developed and used to test the responses of sutures to controlled loading regimes. The loading has been either quasi-static (compressive or tensile) or dynamic (compressive or tensile). Perhaps the classical in vivo example of applying forces to sutures is cranial deformation. This has been practiced by various human groups among e.g. North and South American Indians, Pacific Islanders and various European stocks resulting in e.g. circumferentially or anteroposteriorly deformed crania [78, 79]. While the level of loading 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 described in vitro experiments in which sections of the skull including sutures have been placed and loaded in a dish. These controlled experiments have enabled us to study cellular and morphological changes in the sutures, their main limitations being their in vitro nature, i.e., lacking blood supply and surrounding anatomical structures, and alteration of the overall mechanics of the tissues. One early study that used such an approach was by Meikle et al. [80] on a rabbit model. This was followed by several other groups [81–85]. See the review by Alaqeel et al. [86] for a detailed summary of studies of in vitro loading on sutures (and also in vivo studies). These authors summarized various changes in e.g. protein level, growth factor expression, and extracellular matrix due to the mechanical forces.

A relatively large body of literature has also described in vivo studies in which various sutures have been subjected to different loading regimes and durations. Table 11.3 summarizes some of the key in vivo experiments to the best of our knowledge. These studies, together with the in vitro studies, demonstrate that external tension across sutures up-regulates sutural cell proliferation, increasing the number of cells and their macroscopic width. A quasi-static tensile force seems to have a limited effect [87]; dynamic loading seems to have a larger and perhaps a longer-lasting effect. Kopher and Mao [88, 89] showed that both tensile and compressive cyclic loading can also enhance suture maintenance. Nonetheless, our understanding of the effects of various parameters in such studies (loading duration, frequency, etc.) is still limited and is largely based on the pioneering studies of Mao's team.

11.5 Discussion

The chapter has provided a short summary of the literature on the biomechanics of sutures. The wider literature is not covered here and readers are encouraged to research further. For example, a number of studies have focused on modeling and understanding sutural morphologies [105–107], and there is a wider literature on using FE to address various clinical conditions associated with the craniofacial system. Overall, we feel that this chapter is 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 sutures. Perhaps further studies can use this technique to quantify changes in the mechanical properties of sutures during 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 geometric, morphometric, finite element, machine learning and experimental techniques can be a powerful approach to addressing various non-clinical questions (see e.g., [108]). External loading studies have so far mainly focused on normal sutures; applying same methods 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 treating conditions such as craniosynostosis.

There is no doubt that the whole field of suture mechanobiology has shown immense progress during the past 30 years, advancing our fundamental understanding of this topic. We have already seen several examples that have found their way from basic scientific research to clinical practice. For example, spring-assisted

Table 11.3 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])

Author	Animal	Age	Suture	Level of loading	Duration	Q-static or dynamic
Cleall et al. [92]	Macaque	P90-120	Midpalatal	4 mm expansion achieved in 2 weeks then 2 mm at 4 weeks interval up to 12 weeks	Several intervals from 2 to 36 weeks	Q-static tension
Elder and Tuenge[93]	Macaque	NK	Several sutures	700 Gmat 40° 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	2 mm deflection was induced in a wire frame that was placed across the sagittal suture	Various intervals from 2 h to 42 days	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	50–75 g , 150–175 g and 250–300 g was applied via a helical spring (made from stainless steel) across the maxillary incisors	12 h; 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 3.97 mm distraction was applied to the coronal suture over 42 days	Twice per week for 6 weeks - P28-P70	Q-static
Bradley et al. [98]	Lamb	85–95 days gestation	Coronal	1 mm 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	65 g expansion was applied across the sagittal suture	For 15, 30 and 50 h	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

(continued)

Table 11.3 (continued)

Author	Animal	Age	Suture	Level of loading	Duration	Q-static or 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	20 min/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)	20 min/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	800–1000 μm strain (tensile) was applied to the nasofrontal at 2–3 Hz	30 min/day for 5 days	Dynamic

NK: not known to us; Q-static: quasi-static cranioplasty is becoming a popular treatment option for managing sagittal craniosynostosis (see e.g., [111]), early studies during the 1970s having applied the same concept to various animal models. Large bodies of ongoing research e.g. in the fields of tissue engineering and gene therapies (e.g., [112–114]) can potentially revolutionize the treatment of craniofacial conditions in years to come.

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