Automatic artificial intelligence-based detection of cranial deformity in infants: Clinical validation of a novel smartphone tool

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This thesis is dedicated to my grandmother, Everdina Giesen Nymark, without whose love and support I never would have made it this far. Your commitment to family and your passion for life continues to inspire me every day. I wish you were here to see what comes next.

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Abstract

Positional plagiocephaly is a form of infantile cranial deformity with important aesthetic implications. Pronounced occipital flattening, ipsilateral ear shift and frontal bossing are the primary clinical findings, with more severe cases leading to facial asymmetry. When detected in a timely manner, positional head deformities are generally reversible with treatment (typically repositioning, physical therapy, and/or helmet therapy). The incidence of positional plagiocephaly has increased steadily since the 1990s, spurring an increase in research surrounding long-term sequelae and treatment options. Although positional plagiocephaly is known to not affect a child's neurocognitive development, there is substantial evidence suggesting that earlier diagnosis leads to substantially improved treatment outcomes (such as obviating the need for helmet therapy), reducing or eliminating facial/cranial asymmetry and social stigmatization later in life. Overall, the goal of this work is to gain a greater understanding of the current diagnostic best-practice for positional plagiocephaly and establish the clinical performance of a novel artificial intelligence (AI)-based diagnostic tool. These goals are accomplished through comprehensive literature review and a prospective multi-site clinical validation study. Firstly, we aimed to quantify the importance of early diagnosis in positional plagiocephaly. Through an in-depth literature review, it was demonstrated that earlier diagnosis (by as little as 2-3 months) led to substantial improvements in the financial, emotional, and clinical implications of a plagiocephaly diagnosis. The results described in this manuscript highlight the importance of early diagnosis and management in positional plagiocephaly and informs diagnostic modality selection within a given clinical context. Next, it was important to understand the current landscape for diagnostic modalities that may support physicians in accomplishing earlier diagnosis of positional plagiocephaly. A systematic review revealed 5

diagnostic modalities (anthropometry, plagiocephalometry, 3D laser scanning, digital photographic, and 3D photogrammetry) described in the literature, along with a significant upwards trend in the publication of studies involving artificial intelligence and smartphones after 2017. We also present a novel, AI-based diagnostic tool with strong clinical performance. A clinical validation study was conducted at 2 sites (the newborn nursery at the Royal Victoria Hospital and the craniofacial surgery clinic at the Montreal Children's Hospital) to evaluate the clinical performance of said AI-based diagnostic tool for positional plagiocephaly. Infants <12 months old were recruited and birds-eye-view photographs of their heads were taken with an iPhone 7 Plus, which were subsequently run through an AI algorithm. AI output included a contoured image of the child's head, automatically calculated cranial indices, and a clinical decision on diagnosis (normal, plagiocephaly), sidedness (left, right, brachycephaly), and severity (mild, moderate, severe). Statistical analysis on the AI output revealed strong performance as compared to a gold standard clinical evaluation from an experienced pediatric craniofacial surgeon. Ultimately, this work lays the foundation for future investigation into the optimization of smart diagnostic tools, giving insight into the potential impact such tools may have in the community when deployed on a larger scale.

Résumé

Évaluation d'une application mobile alimentée par l'IA pour détecter la plagiocéphalie positionnelle chez les nourrissons

La plagiocéphalie positionnelle est une forme de déformation crânienne infantile ayant des implications esthétiques importantes. L'aplatissement occipital prononcé, le déplacement de l'oreille ipsilatérale et le bossage frontal sont les principales constatations cliniques, les cas les plus graves entraînant une asymétrie faciale. Lorsqu'elles sont détectées à temps, les déformations positionnelles de la tête sont généralement réversibles grâce à un traitement (généralement le repositionnement, la physiothérapie et/ou le port d'un casque). L'incidence de la plagiocéphalie positionnelle n'a cessé d'augmenter depuis les années 1990, ce qui a suscité une augmentation des recherches sur les séquelles à long terme et les options de traitement. Bien que l'on sache que la plagiocéphalie positionnelle n'affecte pas le développement neurocognitif de l'enfant, il existe des preuves substantielles suggérant qu'un diagnostic plus précoce permet d'améliorer considérablement les résultats du traitement (par exemple en évitant la nécessité d'une thérapie par casque), de réduire ou d'éliminer l'asymétrie faciale/crânienne et la stigmatisation sociale plus tard dans la vie. Dans l'ensemble, l'objectif de ce travail est de mieux comprendre les meilleures pratiques actuelles en matière de diagnostic de la plagiocéphalie positionnelle et d'établir la performance clinique d'un nouvel outil de diagnostic basé sur l'intelligence artificielle (IA). Ces objectifs sont atteints par le biais d'une revue exhaustive de la littérature et d'une étude prospective de validation clinique multi-sites. Tout d'abord, nous avons cherché à quantifier l'importance du diagnostic précoce de la plagiocéphalie positionnelle. Grâce à une analyse approfondie de la littérature, il a été démontré qu'un diagnostic précoce (de 2 à 3 mois seulement) permettait d'améliorer considérablement les conséquences financières,

émotionnelles et cliniques d'un diagnostic de plagiocéphalie. Les résultats décrits dans ce manuscrit soulignent l'importance d'un diagnostic et d'une prise en charge précoces de la plagiocéphalie positionnelle et éclairent le choix des modalités de diagnostic dans un contexte clinique donné. Ensuite, il était important de comprendre le paysage actuel des modalités de diagnostic qui peuvent aider les médecins à réaliser un diagnostic précoce de la plagiocéphalie positionnelle. Une revue systématique a révélé 5 modalités de diagnostic (anthropométrie, plagiocéphalométrie, balayage laser 3D, photographie numérique et photogrammétrie 3D) décrites dans la littérature, ainsi qu'une tendance significative à la hausse dans la publication d'études impliquant l'intelligence artificielle et les smartphones après 2017. Nous présentons également un nouvel outil de diagnostic basé sur l'IA présentant de solides performances cliniques. Une étude de validation clinique a été menée sur 2 sites (la pouponnière des nouveau-nés de l'Hôpital Royal Victoria et la clinique de chirurgie craniofaciale de l'Hôpital de Montréal pour enfants) pour évaluer la performance clinique dudit outil de diagnostic basé sur l'IA pour la plagiocéphalie positionnelle. Des nourrissons âgés de moins de 12 mois ont été recrutés et des photographies de leur tête avec vue plongeante ont été prises avec un iPhone 7 Plus, qui ont ensuite été soumises à un algorithme d'IA. Les résultats de l'IA comprenaient une image de la tête de l'enfant, des indices crâniens calculés automatiquement et une décision clinique sur le diagnostic (normal, plagiocéphalie), le côté (gauche, droit, brachycéphalie) et la gravité (légère, modérée, sévère). L'analyse statistique des résultats de l'IA a révélé une forte performance par rapport à une évaluation clinique de référence effectuée par un chirurgien cranio-facial pédiatrique expérimenté. En fin de compte, ce travail jette les bases d'une recherche future sur l'optimisation des outils de diagnostic intelligents, donnant un aperçu de l'impact potentiel de tels outils dans la communauté lorsqu'ils sont déployés à plus grande échelle.

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Contribution of Authors

Ayden Watt led all research presented in this Thesis and was involved in all aspects of manuscript preparation. The protocols, searches, and data analyses presented in Chapter 2 and 3 were designed and executed by Ayden Watt. He developed, submitted for approval, and subsequently coordinated the REB approved study that was implemented and culminated in the manuscript presented in Chapter 4. All data analysis presented in Chapter 4 was likewise conducted by Ayden Watt. Specifics on the contribution of various authors to the included manuscripts is detailed below.

Chapter 2: Ayden Watt conceptualized and designed the study, designed the data collection instruments, collected data, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Abdulaziz Alabdulkarim reviewed and revised the manuscript; Drs Gilardino and Lee supervised data collection, reviewed and revised the manuscript, and critically reviewed the manuscript for important intellectual content.

Chapter 3: Ayden Watt conceptualized and designed the study, designed the data collection instruments, collected data, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Zammit conceptualized and designed the study, designed the data collection instruments, collected data, and reviewed and revised the manuscript; Drs Gilardino and Lee supervised data collection, reviewed and revised the manuscript, and critically reviewed the manuscript for important intellectual content.

Chapter 4: Ayden Watt conceptualized and designed the study, obtained institutional review board approval, recruited all patients, collected patient data and all clinical images, conducted all data analysis, interpreted results, drafted the initial manuscript, and reviewed and revised the manuscript. Drs Gilardino and Lee aided in the study design and institutional review board approval, supervised data collection, reviewed and revised the manuscript, and critically reviewed the manuscript for important intellectual content.

The manuscripts presented in this thesis are identical to the published or submitted version and are presented in their entirety as independent elements. These manuscripts are subsequently unified with bridging texts which forge the collection of independent works into a cohesive whole.

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Supplemental Figure 1: Data collected from the Newborn Nursery was often poorly illuminated with background conflicts, increasing the difficulty of obtaining an accurate cranial contour.

Abbreviations:

2D: 2 Dimensional

3D: 3 Dimensional

AI: Artificial Intelligence

CI: Cephalic Index

CT: Computed Tomography

CVAI: Cranial Vault Asymmetry Index

FZ-EU: Frontozygomaticus to Eurion measurement

LOE: Level of Evidence

NHS: National Health Service

OCLR: Oblique Cranial Length Ratio

PACS: Picture Archiving and Communication System

PCM: Plagiocephalometry

QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies

1 – Introduction

Positional plagiocephaly, a disease characterized by cranial deformation from prolonged pressure on the skull, is one of the many pathologies that pediatricians and physicians look for during well-baby visits in the first year of a child's life.[1] Typically it will be identified thanks to the characteristic presentation of a parallelogram shaped cranium, caused by occipital flattening (unilaterally or bilaterally), frontal bossing, and an ipsilateral ear shift (± facial asymmetries). While positional plagiocephaly is not known to affect brain development, it can cause permanent cosmetic deformity, noticeable facial asymmetry, malocclusion leading to orthodontic problems in permanent dentition, and is associated with stigma later in life.[2] Careful monitoring in the first months of life is essential to detecting and treating positional plagiocephaly. An infant's skull begins to fuse at 12 months, limiting the potential for treatment, including physiotherapy or helmet therapy, if the condition is not detected in a timely manner.[3] Correspondingly, research efforts in the last 20 years have targeted diagnostic methods for positional plagiocephaly with the goal of creating a new modalities which can supersede the existing gold standard; simple visual assessment.

Unfortunately, no such technology has yet been adopted. Although a variety of diagnostic modalities have been published in the literature, they have failed to provide sufficient clinical performance in conjunction with low cost, ready availability, and ease of use. This limits the widespread adoption of a given modality into practice.

A new concept, bolstered by technological advances in recent years, incorporates artificial intelligence (AI) into standardized (and easily obtainable) clinical images. AI has already been embraced by certain specialties within medicine, such as radiology.[4-6] Machine learning, a subtype of AI, poses as an ideal diagnostic tool. By "training" machine learning algorithms on large

datasets, software can be developed that allows input data (such as the aforementioned clinical images) to be evaluated for a diagnosis and stored.[7]

Correspondingly, the objective of this work was to ask the following questions:

1. Can an AI software detect clinically significant positional plagiocephaly?
2. How does an AI software's diagnostic ability for positional plagiocephaly compare to a gold standard clinical evaluator (pediatric craniofacial surgeon)?

Chapter 2 - Practical Review of the Cost of Diagnosis and Management of Positional Plagiocephaly

2.1 – Title Page

Practical Review of the Cost of Diagnosis and Management of Positional Plagiocephaly

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2.2 – Abstract

Background: Positional plagiocephaly has garnered increased research interest since the introduction of the Back to Sleep campaign in the 1990's, and the subsequent increase in infants with cranial deformity. Research has focused on treatment outcomes and developing new modalities to address asymmetric heads. Little attention has been given to the cost of treatment and diagnosis; this manuscript aims to summarize the literature and provide an overview of the costs associated with a diagnosis of positional plagiocephaly.

Methods: A literature review was performed by searching PubMed and Ovid Embase to identify studies pertaining to the "cost" of plagiocephaly diagnosis or treatment through direct financial factors, disturbance to daily routines (i.e. through treatment prolongation), or related stress.

Results: 29 peer-reviewed studies were included. Treatment options for plagiocephaly are stratified by severity and age of diagnosis, with different pathways available to treat different stages of asymmetry. The common factor across all treatment modalities is that earlier diagnosis unequivocally leads to better aesthetic outcomes and shorter treatment times. This leads to lower costs for treatment, a lower stress burden for parents, and lower costs for the healthcare system in the future through reduction of long-term effects. Our theoretical cost model suggests that early diagnosis at 4 months can lead to a treatment cost of $1295, as compared to $5195 for detection of deformity at or after 6 months.

Conclusions: The dramatic cost disparity between early and late diagnosis highlights the need for reliable methods to accurately detect cranial deformity early in an infant's life.

2.3 – Introduction

It is well established that humans have an aesthetic preference for symmetry.[1] Unsurprisingly then, parents express concern over perceived asymmetry in their children's heads. Unfortunately, the incidence of such asymmetries has been on the rise since the 1990s. Following the introduction of the Back to Sleep campaign, designed to combat sudden infant death syndrome, the prevalence of positional plagiocephaly in infants has risen to above 40%.[2–4] Caused primarily by prolonged external force to the developing skull, positional plagiocephaly is characterized by visible cranial deformity and associated facial asymmetry.[5] Cranial shape can be affected along a spectrum of locations and severities; in the case of the Back to Sleep campaign, infants spend too much time in the supine position, leading to occipital flattening and frontal bossing.[6,7] Mild plagiocephaly will typically present as a slight occipital flattening, while moderate and severe deformities progressively lead to more pronounced occipital flattening (localized to one side or bioccipitaly), the addition of frontal bossing, and ipsilateral ear shift as the head takes on a more "parallelogram" like shape. Additional risk factors for positional plagiocephaly include prolonged/ frequent time in swings or car seats, delayed motor development, and obesity; asymmetric cranial molding can also occur in utero or during birth.[8-12]

Independent pathologies may accelerate the development of positional preferences and resultant plagiocephaly; one study reported torticollis as a clinical finding in more than 90% of infants diagnosed with positional plagiocephaly.[13] Despite the primary concern with positional plagiocephaly being aesthetic, there are concerns for long- term effects when the condition is left untreated. These include orthodontic problems in permanent dentition, visual field restriction, jaw asymmetry, muscular problems, and stigma later in life.[11,14] Positional plagiocephaly is not

traditionally thought to affect cognitive development, though studies have shown that it can be associated with decreased cognitive and academic measures as severity increases.[15]

Infantile screening for cranial deformity is a standard part of well-baby check-ups to ensure healthy development. In many cases, no intervention is needed to correct the deformity; as infants gain control of head movement, cranial shape often normalizes.[16–18] The clinical treatment pathways to manage plagiocephaly are the source of considerable debate, but the value of early diagnosis in managing the condition is well accepted. Cranial sutures start to fuse at 6 months of age, and initiation of treatment before this milestone is crucial to obtaining good clinical outcomes.[19] Despite acceptance of early diagnosis as an important clinical goal, little research has been done to evaluate the cost benefit of an early plagiocephaly diagnosis. This review aimed to summarize the evidence for a reduced cost burden when positional plagiocephaly is diagnosed and treated earlier in life.

2.4 – Methods

A literature review was performed by searching PubMed and Ovid Embase for relevant studies using the search terms “plagiocephaly” AND (“treatment” OR “diagnosis” OR “cost”). Article titles and abstracts were reviewed to ensure they provided information pertaining to the “cost” of plagiocephaly diagnosis or treatment through direct financial factors, disturbance to daily routines (ie, through treatment prolongation), or related stress. Additional articles were screened from cited references. Only English language articles were included.

2.5 – Results

The search returned 636 results. Following individual title and abstract review, 29 articles were included in the review and analyzed for relevant content. Collected data were synthesized into

dominant themes to present a comprehensive review of the literature and to compile evidence on the benefits of earlier diagnosis in plagiocephaly patients.

Clinical Management

Clinical management of cranial deformity is typically stratified by severity, with multiple modalities available to treat varying degrees of plagiocephaly. Treatment strategies are further broken down into passive (repositioning) and active (physiotherapy, cranial remolding therapy, and surgery) modalities. Upon initial observation of asymmetry or deformity by the parents or the pediatrician, the first-line treatment plan is simple repositioning and an increase in tummy time for the infant to decrease pressure on the affected side of the skull.[11,20,21] As plagiocephaly is often accompanied by congenital muscular torticollis, physical therapy is also indicated, with a focus on supporting musculoskeletal development and manipulating tissue to relieve strains causing cranial deformity.[11,22,23] Surgery for release of muscular torticollis is occasionally indicated for cases resistant to physical therapy, and generally only after 12 months of age. From the age of 4–6 months, treatment is guided by severity. Infants affected by mild-to- moderate plagiocephaly (Fig. 1A, B) will be treated with repositioning and/or physical therapy, whereas infants showing severe positional plagiocephaly (Fig. 1C) will often be referred to an orthotic specialist or a craniofacial team to initiate helmet therapy.[5,11,24] Although its use is not universally accepted in the literature, helmet therapy has been shown to correct asymmetry more efficiently than repositioning alone.[10] By the age of 6 months, children with persistent, significant plagiocephaly that did not respond to conservative treatments are frequently sent for helmet therapy, as well as moderate-to-severe cases that present late (at or after 6 months).[5,11,25] Later initiation of helmet therapy treatment generally decreases the improvement in cranial symmetry. Although helmet therapy can have some beneficial effects even at advanced ages (eg,

after 10 months), substantial decreases in cranium and cranial suture plasticity, as well as the decreased rate of brain growth after 12 months of age, lead to much poorer treatment outcomes than in those who initiate treatment early.[5,26,27]

Treatment Burden

Cohort data for repositioning therapy recommend that infants get at least 10–15 minutes of supervised tummy time three times per day.[28] As the definite first-line treatment for cranial deformity, repositioning has the potential to significantly improve head shape without resorting to active treatment.[11,20,21] Repositioning redistributes the repetitive forces that may be applied to an infant's head while they sleep to encourage natural correction of the asymmetry. Repositioning can be prescribed by pediatricians and family physicians while requiring minimal effort on behalf of the infant's caretakers. It is preferable to "watchful waiting" and does not require additional specialist follow-up, which can be inconvenient and costly to the family.[29] Physical therapy treatment approaches to plagiocephaly are still heavily debated. Although its effectiveness at correcting cranial deformity is well documented, there is a lack of consensus for a singular effective treatment.[30] One study by Di Chiara et al saw success with a standardized regimen of 16 weekly 40-minute physical therapy sessions.[22] With the US national cost of physical therapy averaging to $75, Di Chiara's standardized treatment plan would entail a cost of approximately $1200, of which a variable amount may be covered depending on the type of insurance coverage a family has. Thus, the out-of-pocket cost borne by patients and their families can vary widely.[31]

The American Association of Physical Therapy recommends that patients fitted with cranial orthoses receive follow-up 1 week after fitting and every 2 weeks thereafter.[32] Certain orthotics, such as the DOC Band, require adjustment every week.[33] Usually ranging from $1500 to $3000,

the cost of the cranial orthotic typically includes the helmet and required follow-ups for helmet adjustments. Most cranial orthotics "grow" with the infant, thanks to progressive and planned removal of the foam lining the orthotic.[34] However, significant cranial growth can necessitate the need for a second, and sometimes third, orthotic.[35] As with physical therapy, insurance coverage for helmet therapy is variable; the true cost of treatment will need to be assessed on a case-by-case basis.[11] In the United States, caregivers for affected infants had to cover costs themselves in 45.1% of cases. Of those that could submit the costs of helmet therapy to health insurance, 36.1% reported conflicts with the health insurance company regarding the refund of costs.[36] Third party insurance companies often refuse to cover treatment for positional plagiocephaly, arguing that the deformity is purely cosmetic and that active treatments (like helmet therapy) are not substantially better than parental repositioning.[11,37] One study by Lam et al analyzed the degree of treatment compliance according to patient subgroups and found that families with public insurance were less likely to adhere to the recommended treatment than families with private insurance (80.2% versus 89.6%).[38] The authors do not discuss the cause, but one possibility is a lack of coverage for required follow-ups. The consensus is that coverage for low-income Americans is insufficient to support multivisit treatment plans, which considerably affects treatment accessibility and can lead to the development of more severe deformities in low-income households.[31] This phenomenon has previously been well documented for medication nonadherence in low-income uninsured patients with chronic conditions.[39] Furthermore, Junn et al recently reported that patients on Medicaid were 1.30 times more likely to have delayed presentation for helmet therapy consultation than those with commercial insurance, whereas patients in the highest and second highest income quartiles were respectively 1.55 and 1.45 times more likely to receive helmet therapy following consultation.[40] These

findings further highlight the clear diagnosis and treatment discrepancies found in different socioeconomic strata.

Emotional Toll

Initial detection of cranial deformity is usually noted in the third or fourth month of life by the child's parents or pediatrician. A conclusive diagnosis can be expected to be made within a month of the initial detection, with rapid initiation of preclinical passive treatment measures (ie, repositioning). Initial presentation of infants with a cranial deformity to craniofacial specialists is not until almost six months of age (average 5.8 month), with an average delay of 3.33 months between the initial recognition of deformity and first specialist presentation.[41] Kluba et al suggest that this places increased pressure on parents to make an immediate decision, as the outcomes of treatment modalities such as helmet therapy are heavily reliant on early initiation of a treatment regimen.[41] Personal strain on caregivers is rarely considered in the literature, but represents an important component of the burden of diagnosis. Increased caregiver stress levels can play a significant role in the degree of treatment compliance (and thereby treatment efficacy). A distinct study by Kluba et al evaluated factors related to poor treatment compliance.[36] They discovered that more than 80% of parents had been affected by treatment related issues; the most commonly cited were financial cost, disputes with health insurance, concern for the child, time spent bringing the child to and from the clinic, and social conflicts.[36] Martiniuk et al reported that in their survey, parents of a child with moderate-to-severe plagiocephaly expressed sadness that they had not addressed the flat head sooner and felt sorry for their child when they were forced to wear an orthotic helmet around the clock; typical regimens require the child to wear the helmet 23 hours a day, every day, for months at a time.[42,43] Importantly, helmet therapy has been shown to not affect infant quality of life.[42] Discrepant and unclear clinical pathways for plagiocephaly

form an additional source of parental emotional burden. As physicians are not in agreement on the most appropriate treatment paths for cranial deformity, parents can be confused by potentially contradicting information.

The Benefit of Early Diagnosis

The true cost of a diagnosis is measured by a combination of financial factors, disturbance to daily routines, and related stress. Prolonged treatments cause greater upset in the lives of patients' families as they continue to bear the burden of care. As the numbers of plagiocephaly patients rise, it becomes ever more important to optimize the treatment pathway for these patients.[5] Table 1 illustrates the theoretical financial and clinical outcome dis- parity between early diagnosis with successful physical therapy treatment and late diagnosis with unsuccessful physical therapy requiring subsequent conversion to helmet therapy.[22,35,44,45] Research into effective physical therapy programs is crucial to the optimization of multidisciplinary treatment. The literature shows that age and degree of severity are essential factors in determining treatment duration and outcomes for patients diagnosed with plagiocephaly. Di Chiara et al reported that their physical therapy program led to positive improvements in 58.3% of the population for the Cranial Proportional Index/Cephalic Ratio and 70.8% for the cranial vault asymmetry index (CVAI), with the highest rate of improvement found in infants under the age of 8 months.[22] Specifically, they noted that almost all reference measurements were most improved in infants aged 5–8 months, with no significant difference in treatment efficacy between infants aged 1–4 months and 5–8 months.[22] Van Vlimmeren et al's randomized control trial returned similar results; the occurrence of severe deformational plagiocephaly in infants that underwent physical therapy was reduced by 46% and 57% at 6 and 12 months of age, respectively.[28]

Physical therapy plays a further role supplementing less conservative techniques. In a study by Steinberg et al, complete correction of cranial deformity was achieved in 77.1% of conservative treatment patients (repositioning ± physical therapy); 15.8% required transition to helmet therapy, and 7.1% ultimately had incomplete correction.45 Furthermore, complete correction was achieved in 94.4% of patients treated with helmet therapy as first-line therapy and in 96.1% of infants who received helmets after failed conservative therapy.[45] The authors found that the risk of failure for both conservative and helmet molding therapies increased with age; the younger than 3 month, 3–6 month, 6–9 month, and older than 12 month age categories demonstrated progressively increasing failure rates.[45] Conservative therapy was two times more likely to fail at older than 12 months when compared with younger than 3 months, and helmet therapy was greater than three times more likely to fail with the same age groups.[45]

Several studies have made recommendations for an ideal helmet therapy start date for plagiocephaly patients. Han et al found that initiation of helmet molding therapy between the ages of 3–5 months yielded consistent results, but that initiation beyond 6 months led to significantly decreased rates of CVAI improvement and significant increases in duration of therapy.[44] Han et al further demonstrated that starting helmet therapy at 3 months could as much as halve treatment times compared with their 8-month-old initiation group.[44] In a study by Hinken et al, the average CVAI improvement with helmet therapy decreased by 36% between the 4–6 month group and the 7–9 month group.[26] Graham et al concurred reporting that both treatment duration and treatment outcomes were improved by earlier initiation of cranial molding therapy.[46] Finally, Kluba et al's study resulted in infants less than 6 months old having 4 week shorter helmet therapy treatment time and greater reduction of asymmetry than those in the more than 6 months group.[47] Furthermore, the aver- age infant in the more than 6 month group was not

able to achieve normal values for CVAI, which were attained by the younger group.[47] Importantly, decreased effectiveness does not invalidate the commencement of therapy at an advanced age. Several studies have shown that although failure rates are higher and treatment duration increases, therapy can still have a positive effect on head shape.[26,27]

In addition to early diagnosis, a high degree of treatment compliance is essential to obtaining positive clinical outcomes. For infants undergoing orthotic helmet therapy, this can mean wearing the helmet up to 23 hours per day, while patients prescribed active repositioning depend on a high degree of treatment compliance for parents following standard instructions.[48] Physiotherapy also typically requires multiple visits, requiring commitment from the parents to bring their children to and from appointments.[22]

2.6 – Conclusion

Early identification of positional plagiocephaly plays an important role in lowering the monetary and intangible costs of the diagnosis. Earlier diagnosis has been proven to lead to better outcomes and reduced treatment times, as well as an increased likelihood of compliance with the treatment regimen. Furthermore, the intangible implications of prolonged treatment time due to delayed diagnosis significantly increases the burden on parents, through an increased number of specialist visits, increased likelihood of helmeting, and prolonged emotional strain from caring for the child. The resultant financial and resource burden placed on caregivers and/or the healthcare system is demonstrated in our modeled early versus late diagnosis treatment pathways. In the future, research should be directed at accessible tools that may facilitate early diagnosis of plagiocephaly across all socioeconomic demographics to mitigate the avoidable consequences of late detection.

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2.8 – List of Tables:

Table 1. Cost model for early vs. late diagnosis of positional plagiocephaly

Age (months)	4	4.5	6	6.5	7	8	15	**Final Cost**
Early Diagnosis	Confirmation of moderate plagiocephaly by pediatrician at well-baby visit, initiation of repositioning	Initiation of Physical Therapy (16 weekly sessions of 40 minutes)	Physical therapy is improving cranial deformity	-	Craniofacial specialist confirms plagiocephaly, physical therapy is improving cranial deformity	Physical Therapy treatment completed with acceptable correction of deformity	-	-
Cost	$95	$1200	-	-	$200	-	-	**$1495**
Late Diagnosis	-	-	Confirmation of moderate plagiocephaly by pediatrician at well baby visit, initiation of repositioning	Initiation of Physical Therapy (12 weekly sessions of 40 minutes)	Craniofacial specialist confirms plagiocephaly, physical therapy is unsuccessful, recommends helmet therapy	Helmet therapy initiated; average treatment requires 2 helmets	Conclusion of helmet therapy, <20% chance for complete correction of deformity	-
Cost	-	-	$95	$900	$200	$2000 x 2 helmets	-	**$5195**

2.9 – Bridging Text

The literature review described above highlights the variability in treatment pathways for infants with positional plagiocephaly, in accordance with age at time of diagnosis and severity of deformity. Furthermore, the substantial financial discrepancy between a timely diagnosis and one that is delayed by several months is elucidated, with a predicated cost of treatment approximately 3.5 times greater in infants that begin treatment later in life. Finally, a greater appreciation for the intangible costs of diagnosis is gained through a comprehensive review of factors affecting caregivers; heightened stress levels, substantial treatment compliance requirements, time away from work, and social implications were all found to be worsened when a diagnosis is made later in life. Ultimately, the literature review concludes that supporting earlier diagnosis of plagiocephaly would be an effective way to lower the burden (financial and emotional) on caretakers, improve treatment outcomes, and lower costs to the healthcare system. Accordingly, the following systematic review was conducted to summarize currently available diagnostic modalities for positional plagiocephaly, observe trends in innovation, and provide a comprehensive overview of clinically available tools. A particular emphasis was placed on those tools that may support earlier diagnosis of positional plagiocephaly.

Chapter 3 – Novel Screening and Monitoring Techniques for Deformational Plagiocephaly: A Systematic Review

3.1 – Title Page

Novel Screening and Monitoring Techniques for Deformational Plagiocephaly: A Systematic Review

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3.2 – Abstract

Context: Deformational plagiocephaly is a common diagnosis encountered by pediatricians in the first year of life. Subjective clinical examination and documentation is the most common method for identifying and monitoring the evolution of head shape and in determining treatment or the decision to refer to a specialist.

Objective: In this systematic review (PROSPERO; CRD42021224842), we aim to compile the evidence for non-radiographic screening and monitoring modalities for deformational plagiocephaly in infants to support pediatricians in achieving earlier diagnosis and more objective monitoring.

Data Sources: A systematic review of the literature was conducted using OVID Medline, EMBASE, and Web of Science.

Study Selection: Articles pertaining to the use or evaluation of diagnostic modalities for plagiocephaly in infants published between January 1990 and August 2021.

Data Extraction: Data on diagnostic accuracy, time-to-diagnosis, reliability, and outcomes for each modality were collected as available by two independent reviewers.

Results: 22 studies were included. We identified 5 unique head shape monitoring technologies: anthropometry, plagiocephalometry, 3D laser scanning, digital photographic, and 3D photogrammetry. Smartphone and artificial intelligence integration has increased in plagiocephaly and craniosynostosis screening and monitoring tools.

Limitations: Inconsistent reporting both inter- and intra-modality hindered meaningful comparison between screening tools. Substantial heterogeneity in measured outcomes, study design, and population size made cross-study comparisons difficult.

Conclusions: A growing list of quantitative diagnostic modalities for head shape monitoring exist that are becoming accessible to pediatricians. The introduction of artificial intelligence to 3D photogrammetry and digital photography with easy-to-use smartphone applications seems promising for future diagnostic efficiency.

3.3 – Introduction

Deformational plagiocephaly is the leading cause of head shape abnormalities in children, with mild cases affecting approximately 40% of infants under the age of 1 year.[8] Severe cases of deformational plagiocephaly are much less frequent, and in exceptional cases may require surgical intervention. Though it spares a child's neurocognitive development, deformational plagiocephaly can cause significant cosmetic deformities, such as facial asymmetry, eventual malocclusion needing orthodontic treatment and social stigmatization later in life.[2] Most often, it is detected by the child's parents or pediatrician through simple visual assessment.[9] Subsequent monitoring of abnormal head shape is crucial, as the progression of deformity despite conservative treatment for deformational plagiocephaly can be indicative of the need for additional intervention (such as treatment of persistent torticollis) or an undiagnosed sutural fusion (craniosynostosis) requiring surgical treatment.

The most common monitoring strategy remains clinical examination including documentation of head circumference. Combined with the interval between visits, the subjective nature of clinical examination for the monitoring of head shape improvement or deterioration remains a challenge. As such, determining if and when to refer patients for additional treatment (physiotherapy for persistent torticollis) or specialty consultation (persistent plagiocephaly, possible craniosynostosis), remains a therapeutic dilemma.

To that end, there are a number of new, readily available imaging modalities that may provide pediatricians with objective measures of head shape progression and assist in diagnostic decision-making. Technological advances in the medical field, bolstered by parallel advancements in hardware, computing power and artificial intelligence (AI) capability, have introduced new diagnostic methods capable of tracking head shapes.[10] Older quantitative methods of monitoring

head asymmetry demonstrated acceptable accuracy but were expensive and/or time-consuming as calculations and post-processing were primarily manual. To our knowledge, no recent comprehensive review of the screening and monitoring modalities for deformational plagiocephaly exists to highlight progress in time-to-diagnosis, accuracy, and accessibility. The aim of this study is to compile and evaluate the full complement of diagnostic modalities available to support pediatricians in identifying and monitoring cranial deformity in infants. The overarching goal involves eventual implementation of capable diagnostic support tools to ultimately help guide appropriate treatment and specialist referral.

3.4 – Methods

This systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and was prospectively registered in PROSPERO (CRD42021224842).

Eligibility Criteria

The review included studies involving children or models of children under the age of 18, with a primary focus on infants under 12 months of age. Studies involved comparison or evaluation of diagnostic techniques or technologies (non-radiographic modalities), new diagnostic software analysis systems, pilot/proof-of-concept studies for new diagnostic modalities, or studies comparing diagnostic measurements to determine the most useful head shape parameters. There was no restriction to the type of study design, and only English language studies were considered.

Studies were excluded if they met any of the following criteria: case-report, focus on a diagnostic technique involving radiation, ultrasound, focus on surgical recovery, surgical outcome

evaluation, genetic-based diagnoses, prenatal diagnosis, and intracranial volume quantification. Conference proceedings and abstracts were also excluded.

Search Strategy and Data Sources

A literature search was conducted on November 11th, 2020, in Ovid Medline, Ovid EMBASE, and Web of Science. The search strategy was built using subject headings, keywords, and MeSH terms related to "diagnosis", "screening", "monitoring", "plagiocephaly", and "craniosynostosis". These guiding terms were chosen as those most likely to recommend clinically useful tools and developments for pediatricians. The full search strategy for Ovid Medline and Ovid Embase is detailed in Appendix 1. The search encompassed all publications between January 1990 and August 2021, as developments explored prior to 1990 would no longer be relevant given the pace of technological advancement.

Study Selection and Data Extraction

Records obtained from the initial search strategy (13 857 records) were imported into Endnote X9 for deduplication. The de-duplicated results were imported into Rayyan for screening. Two independent reviewers (A.W. and D.Z.) screened each study for relevance based on title and abstract (level 1 screening). Conflicting decisions were resolved by discussion and consensus among the authors. The full text of each study included after level 1 screening was then acquired and reviewed by the authors to determine final inclusion or exclusion. Any conflicts were resolved by discussion and consensus of the authors.

We followed a descriptive synthesis approach and categorized the included studies by diagnostic modality. Data on diagnostic accuracy, time-to-diagnosis, reliability, and technological

novelty were collected independently by A.W. and D.Z. as available for each included study. Data was then summarized through four key diagnostic domains that best represented developments in the field: shape analysis, reliability, smartphone integration, and automation.

3.5 – Results

The systematic review identified 13 857 articles. 9 349 articles remained after de-duplication; 62 articles remained after title and abstract screening. Full-text review returned a final inclusion of 22 articles spanning 5 diagnostic modalities (Fig 1, Table 1, Table 2). The most frequent modality described in the included studies was photogrammetry (50%). Our review included studies describing the following modalities: photogrammetry (11), anthropometry (2), laser scanning (1), 2D digital photography (7), and plagiocephalometry (1) (Table 1, Table 2, Figure 2).

Risk of Bias

Two authors (A.W. and D.Z.) independently evaluated the risk of bias for all included studies using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (Appendix 2).[11] Of the 22 included studies, 19 were found to be at low risk of bias, while 3 were evaluated as high-risk (Table 3).

Study Characteristics

Included studies were published between 2005 and 2021. The authors of included studies reported on range of outcomes including accuracy, variability, time-to-diagnosis, comparison to gold-standard computed tomography (CT), and patient comfort; reported outcomes varied

significantly by study. Patient age varied from 3 months to 12 years of age. Sample size for clinical studies ranged from 2-339. Six studies used pre-assembled datasets of cranial head images or models to evaluate performance. Ten studies reported sex, five of which reported >50% female participants.

Modalities

Every modality included in this study aims to quantify cranial asymmetry, but all take different approaches (Table 2, Fig, 2). Anthropometry uses calipers and measuring tapes to take assorted measurements of the child's head. These measurements are then used to calculate cranial asymmetry indices (CVAI, CI, OCLR, etc.) which can inform the user of the presence and severity of cranial deformity. Plagiocephalometry uses a thermoplastic band wrapped around the child's head to make a mold that can be traced onto a paper. This trace can then be used to take measurements and calculate asymmetry indices without the child moving around. Digital photography commonly uses a photo taken from a birds-eye-view perspective of the child's head. Measurements can then be taken directly off the photo with manual landmark selection, but new automated methods exist that take automatically calculated asymmetry indices (Fig 3). New digital photography techniques can use smartphones to take photos, and this ease of use translates to new 3D photogrammetric techniques. 3D photogrammetry uses either the slow-motion features on modern smartphones or multi-camera stationary imaging setups. In this method, a 3D image is pieced together from many still photos taken from different perspectives; cranial asymmetry can then be evaluated using 2D anthropometric indices or more complicated 3D indices. Finally, 3D laser scanning uses a stationary or handheld scanner to create a 3D representation of the infant's head. For all image-based modalities (i.e. Photographic, photogrammetric, laser scanning) an

infant's hair presents an important confounder; to minimize its affect, infants are fitted with a nylon cap (with reflective dots in the case of laser scanning).

Shape Analysis

A common theme across all modalities was the ability to characterize head shape. Specifically, quantifiable analysis of skull deformity was highlighted as an important trait in new diagnostic modalities. Shape analysis was divided between 2D methods (anthropometry, plagiocephalometry, digital photography) and 3D methods (laser scanning, photogrammetry). 2D and 3D methods are distinguished by their speed and ability to evaluate multiple imaging planes. Measurements taken from these methods are calculated into indices, such as cephalic index (CI) or cranial vault asymmetry index (CVAI), and used to evaluate the degree of deformity. 3D methods allow the development of more complex indices looking at deformity in multiple planes, but in some instances were found to retain the use of 2D indices.[12-14] Deformational cranial growth is not restricted to the 2D plane, and in some cases may be more accurately diagnosed by 3D methods. Meulstee et al. implemented principal component analysis to determine the mean cranial shape in the normal population and subsequently distinguish deviations from "normal" with 3D reconstructions obtained from photogrammetry.[15] Atmosukarto et al. demonstrated that their novel 3D-based plagiocephaly posterior severity scores were more capable of discriminating plagiocephalic and normal head shapes than 2D measurments.[16] By contrast, Skolnick et al. used non-linear measures of cranial asymmetry from 3D photographs to identify the most capable linear measure, while Barbero-Garcia et al. evaluated the performance of a 3D-photogrammetric method using automatically-derived linear (2D) measurements.[14, 17] Wu et al. (anthropometry) and Van Adrichem et al. (plagiocephalometry) demonstrated that 2D methods were capable of returning

results that correlated with CT-derived measurements ($P > 0.05$ for both studies).[18, 19] Barbero-Garcia et al. demonstrated an accuracy with tolerances below 1.5 mm when comparing 3D-photogrammetry (smartphone-based) to 3D-CT.[17] A later study by Barbero-Garcia et al. combined machine learning-based facial analysis with their 3D-hotogrammetry system to improve cranial measurement in dynamic infants and capture facial asymmetries associated with cranial deformities; the authors concluded that eyes were the most consistently identifiable facial landmarks, though 3D coordinates of facial landmarks were not accurately obtained in 52.9% of cases.[20] Due to equipment cost and the technical skill required to operate the system, 3D photogrammetry and laser scanning are generally centralized at a specialized location.[19, 21-23] Laser scanning and 3D photogrammetry share key characteristics: quick capture times, precise, quantitative data collection, and an ability to track changes in head shape over time.[23] Nonetheless, Nahles et al. found that 3D laser scanning took, on average, more than 3 times longer than an anthropometric measurement.[21] 3D photogrammetry was shown by Aarnivala et al. to not be affected by the age of the infant.[12] Newer technology-based shape analysis methods were highlighted by high accuracy and improved analysis times: Barbero-Garcia presented a 3D-photogrammetric method that returned a diagnostic result in under 5 minutes.[13, 15, 17, 24] One significant consideration in the clinical evaluation of head shape is the differentiation between positional plagiocephaly and craniosynostosis. While Tu et al., Meulstee et al., Porras et al., Agarwal et al. and de Jong et al. all demonstrated that their tools could reliably differentiate varying forms of synostosis from a healthy control, and several of the included studies were able to distinguish positional deformities from a healthy control, this review returned no studies that reported on diagnostic differentiation between positional and synostotic deformities. [15, 22, 25-30]

Reliability

Given that a child may see different physicians at standard "well-visits" during the first few months of life, high inter and intra rater reliability of cranial measurements are important to accurately monitor deformity progression. Anatomical landmarks used in different deformity indices were found to have varying intra rater reliability.[14] Using 3D photogrammetry, Skolnick et al. demonstrated that the contralateral frontozygomaticus to eurion (FZ-EU) measurement was the linear measure that best correlated with overall cranial asymmetry ($r \geq 0.90$).[14] Anthropometry and plagiocephalometry have been shown to return acceptable interrater reliability.[19, 31] When implemented with a well-defined protocol, an anthropometric study led by Wilbrand et al. returned intra and inter observer variabilities of 0.03% (<1.131 mm^2) and 0.5% (<0.182 mm^2), respectively, with 2mm of overall measurement variance.[31] Van Adrichem et al. reported no statistical difference ($P > 0.05$) between a PCM ring off the head and CT-based skull measurements with a plagiocephalometric method.[19] Schaaf et al.'s study concerning a digital photographic method reported inter-observer correlation coefficients of 0.982 and 0.946 for CI and CVAI respectively.[32] In a distinct study by Schaaf et al., multi camera 3D photogrammetric methods (operated by trained specialists in a centralized location) returned an intra-class correlation coefficient of 0.97 for plagiocephaly and 0.98 for brachycephaly.[13] More accessible to front line physicians, two studies by Barbero-Garcia et al. evaluating smartphone-based 3D photogrammetric methods have returned accurate measurements, with standard deviation below 1.4 mm with a 99% confidence and differences in means (for intra- and inter- user tests) below 1mm with a 95% confidence interval.[17, 24]

Smartphone integration

Given the ubiquity of smartphones in the pockets of modern physicians, this review returned very few studies embracing the shift towards mobile optimization of previously specialized tools. Older digital photographic methods requiring dedicated handheld cameras and manual cranial measurements are now superseded by cellphone cameras for use in digital photographic diagnostic modalities.[17, 22] The network connectivity that new smartphones can leverage opens the doors for cloud computing, where the processing of a digital image is sent off to a server that returns a diagnostic output.[17] As evidenced by Barbero-Garcia et al. (2019) and Barbero-Garcia et al. (2020), the implementation of native slow-motion filming in smartphones is capable of automatic, handheld, and accessible photogrammetric 3D modelling.[17, 24] While smartphone-based 3D-photogrammetric methods take longer to scan (< 5 minutes) compared to specialized multi-camera setups (< 1 second), they are significantly more accessible and user friendly, with no requirement for specially trained users.[13, 15, 17, 24]

Automated Diagnosis

Anthropometry and plagiocephalometry, as well as early digital and 3D photography, were limited by their dependence on manual determination of cranial landmarks, introducing error and increasing variability between examiners. Technological advancement has provided a solution for this quandary: automated diagnosis. Automated diagnosis saw a 762% increase in the literature since 2017, with 11/13 studies published since 2017 including a form of automation. Increases in computational ability and the adoption of AI by the medical community has proved promising for automated digital photographic assessment. Since 2017, Agarwal et al. report a testing accuracy of 84.12% for a machine learning model that identifies craniosynostosis; Porras et al. described an algorithm which detected craniosynostosis automatically with 94.74 percent sensitivity and 96.02

percent specificity.[26, 28] It further correctly identified the fused sutures with 99.51 percent sensitivity and 99.13 percent specificity.[28] de Jong et al. also reported a deep learning algorithm for classifying craniosynostosis in which 195/196 (99.5%) stereophotographs were correctly diagnosed.[29] Bookland et al. described their cranial shape classification software, which had an accuracy of 93.3% (95% CI 86.8–98.8; $p < 0.001$), with a sensitivity of 92.0% and specificity of 94.3%.[33] Geisler et al. developed a convolutional neural network to classify synostosis; overall testing accuracy for their model was 90.6%, with higher sensitivity and precision when identifying metopic (100%, 100%) and sagittal (93.3%, 100%) synostosis compared to unicoronal synostosis (66.7%, 100%).[34] Finally, Tu et al. evaluated a support vector machine classifier which obtained a diagnostic accuracy of 91.03% for craniosynostosis, compared to 78.21% when applying methods which used head circumference/CI.[30] While diagnostic times for non-automated methods were not reported in the literature, 3D scans taken with a smartphone returned a diagnostic result in as little as 2 minutes without sensitivity to the user.[17] Notably, all the included automated diagnosis studies highlighted the need for access to larger training data sets as the most significant barrier to improved performance.[22, 25, 26]

3.6 – Discussion

Recent technological advancements have allowed for the development of diagnostic tools to support pediatricians in monitoring head shape that are fast, accurate and reliable. Shape analysis, smartphone integration and automated diagnosis enhanced by AI have all seen considerable development in recent years, with promising potential for further improvement. Pediatricians manage large patient loads, and standard clinical and visual examination techniques lack the ability to accurately monitor changes in head shape. Subtle changes in the deformity over

time can help inform treatment and referral decisions, so reliable and consistent monitoring is crucial to ensure positive neurological and aesthetic outcomes.[1, 35, 36] The result of extrinsic forces on the infants skull in utero or early in life, cranial deformities will often normalize during the first few months of life with appropriate treatment.[3, 37] Increased (monitored) tummy time and physiotherapy are typically prescribed to address external causes such as torticollis; advanced cases may benefit from helmet molding therapy.[3, 38, 39] The effect of these treatments on head development can help distinguish deformational plagiocephaly from true craniosynostosis, and is valuable information for both pediatricians and the specialized craniofacial teams that treat true craniosynostosis. The gold standard diagnostic confirmation for suspected craniosynostosis is cranial 3D-CT.[40-43] It has been reported that outpatient CT exams (i.e. those ordered by non-craniofacial specialists) on patients with cranial deformities return negative findings in 75-80% of cases.[44] Specialists deciding whether patients with unclear clinical presentation should undergo CT would benefit from a tool providing detailed and quantitative history of head shape progression.

Accurate, accessible and quantitative measurement of head shape is the cornerstone of early cranial deformity screening and eventual monitoring. A range of diagnostic modalities meeting these criteria were reported in the literature: anthropometry, plagiocephalometry, digital photography, and 3D photogrammetry. 3D laser scanning was also included in the review, but was found to offer no advantages over much cheaper anthropometric techniques; Nahles et al. recommended that if available, 3D photogrammetry should be used until such time as developments in laser scanning techniques reduce the scanning time and increase the consistency of results.[21] While capable of returning accurate results, manual anthropometric techniques (including plagiocephalometry) have been overtaken by newer modalities taking advantage of

technological developments that automate and speed up diagnosis to support pediatricians in the clinic.[45] In particular, smartphone based digital photographic techniques for shape analysis have a promising future. Digital photos can leverage a modern smartphone's network connectivity to access cloud servers for fast storage and retrieval, allowing physicians to directly compare quantitative (calculated asymmetry index) and subjective (visual head exam) data across multiple patient visits. While smartphone cameras have lower radiometric accuracy than single lens reflex cameras, their ubiquity and portability more than make up for losses in image quality.[46] Despite only being used for head shape analysis since 2019, smartphone cameras have previously been successfully implemented across many medical fields, including plastic surgery for 3D facial scanning, monitoring microvascular responses to physiological provocations in the skin, and augmented reality microsurgical planning for lymphovenous anastomosis.[47-49] The use of slow-motion video-recording on smartphones enables low-cost 3D-photogrametric modelling that is insensitive to use by non-medical users while still providing results comparable to CT.[17] These methods are highly automated and can return results to the physician in as little as 4 minutes.[17] Plain photographs from smartphones can also leverage automatic measurement extraction for fast quantitative results.[22, 26] Accounting for motion is a crucial consideration when dealing with a patient population that has difficulty sitting still, and it will play an important role in the efficacy of future techniques. Particularly in smartphone-rendered 3D models where capture speeds are not instantaneous, innovative and computationally-efficient ways to deal with infant motion are required. Barbero-Garcia et al.'s method accomplished motion-insensitivity by automatically overlapping images using a coded cap and discarding any non-ideal frames.[17] It is important to emphasize that the case for smartphone based diagnostic software is still in its infancy; while new developments are promising for future integration into clinical practice, further refinement is

required for successful, widespread adoption. Current systems supporting the generic diagnosis of head deformity are highly performant, but translation of these tools for the diagnosis of craniosynostosis (a deformity distinguished primarily by internal pathology) will likely require significant databases and a helping hand from AI algorithms. When coupled with improved AI systems, mobile photographic methods have the potential to put automated diagnostic software on par with trained radiologists in physicians' pockets.

The introduction of AI and automation into newer digital photographic solutions has the potential to drive down exam times and further enhances clinical viability.[10, 26] Model performance is dependent on the quality and size of the training set used to instruct it, and there are currently no sufficiently large, high quality training databases for the modalities included in this review.[25, 26, 28-30] There have been promising attempts to artificially expand datasets using a Generative Adversarial Network (a deep learning technique), which outputs data similar (but not the same) as the data input of the network. The method of multiple runs has also proved promising to maximize training on a small dataset.[50, 51] While similar techniques warrant further research, they do not obviate the need for large, annotated, craniofacial databases based on real patient data. Conversely, radiographic imaging has access to massive amounts of data. The implementation of the Picture Archiving and Communication Systems in the USA, Canada, and Europe has provided unparalleled access to clinical imaging datasets.[52, 53] The 2018/19 year alone saw the addition of 44.8 million imaging tests to the NHS PACS in England.[54] Correspondingly, AI has seen greater success and implementation in supporting radiologists; a 2020 study introduced a new AI system for predicting breast cancer in screening mammography's that outperformed all of the expert human readers involved.[55] More relevantly, a machine learning algorithm has been trained to distinguish between types of craniosynostosis on CT scans of patients and return the correct

diagnosis, with a sensitivity of 92.3 percent and a specificity of 98.9 percent.[56] The development of training sets for non-radiographic diagnostic modalities should increase our ability to develop deep learning and convolutional neural network based frameworks for cranial deformity diagnosis. Additionally, expanded datasets will play a crucial role in establishing clinically relevant diagnostic cut-off values for deformational indices. Indicators of craniofacial deformity (CVAI, CI, OCLR, etc.) are based on the 2-dimensional measurements found in anthropometric methods, but 3D models can be evaluated by novel multi-dimensional indicators of cranial deformity.[12, 14-16] To fully leverage the diagnostic ability of AI systems, clinical indicators for cranial deformity need clearly defined diagnostic cut-offs for measurement values.

There are several limitations found in our systematic review. Most notably, there is significant heterogeneity in the presentation and quality of data in studies presenting diagnostic tools, whether as a proof of concept or a validation study. A lack of common performance reporting practices across different modalities creates a challenge in translating results for comparison. Certain modalities, such as 3D laser scanning, were also found to be significantly underreported, despite being highly cited in the literature. A crucial variable in the evaluation of front-line technology integration is time; most of the studies in this review did not report the time required for a given examination. Paired studies also usually neglected to compare patient (infant and parent) preferences.

3.7 – Conclusion

Pediatricians have access to a comprehensive range of tools when evaluating for, and monitoring potential craniofacial deformities. While limited by the reporting practices seen in the literature, substantial evidence exists to support the use of these tools by pediatricians for clinical

monitoring of cranial deformity in infants. There are a multitude of potential diagnostic options, and selection will likely be made on a case-by-case basis depending on resource availability. Regardless of the choice, successful diagnostic tools were all reliable, quantitative, and fast, with newer mobile solutions being increasingly cost-effective. Smartphone-based options, particularly those leveraging AI classification algorithms, hold great promise by placing significant diagnostic power within the pockets of physicians around the world. Particularly for those physicians without easy access to a tertiary care center and craniofacial specialists, future work optimizing mobile diagnostic tools has the potential to significantly improve diagnostic times and consequently, patient outcomes.

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3.9 – List of Figures

Figure 1: Summary of systematic search results

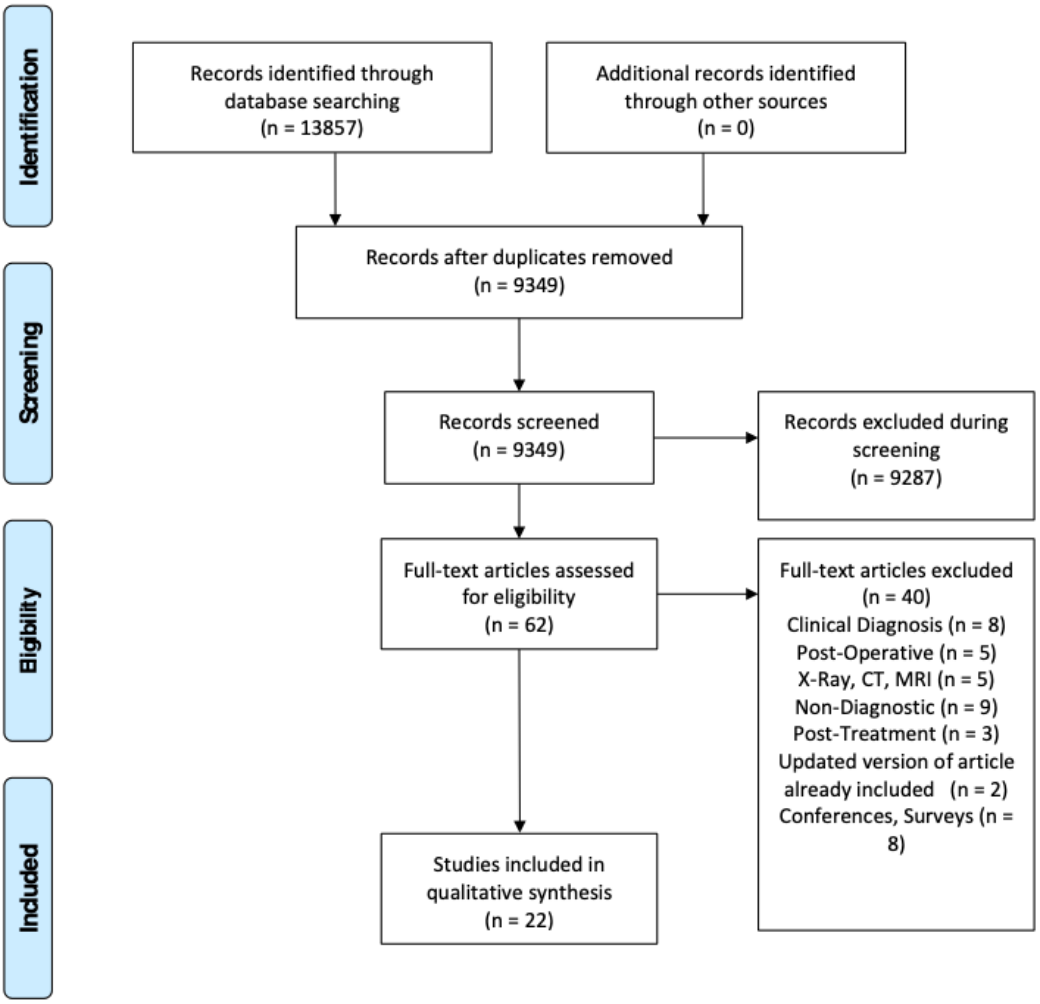


Figure 2: (A) Anthropometric measurement of the head using calipers. (B) Plagiocephalometric measurement of the head using a thermoplastic band and sketching (C). (D) Digital photographic measurement of head shape. (E) Example of cap required for 3D analysis of cranial shape used in 3D laser scanning (F), and 3D photogrammetry (G). (H) Example of cranial measurements obtained from 3D renders of an infant's skull in multiple planes. Panels A-H are being reprinted with permission. Please see **Permissions for Figure 2** for details.

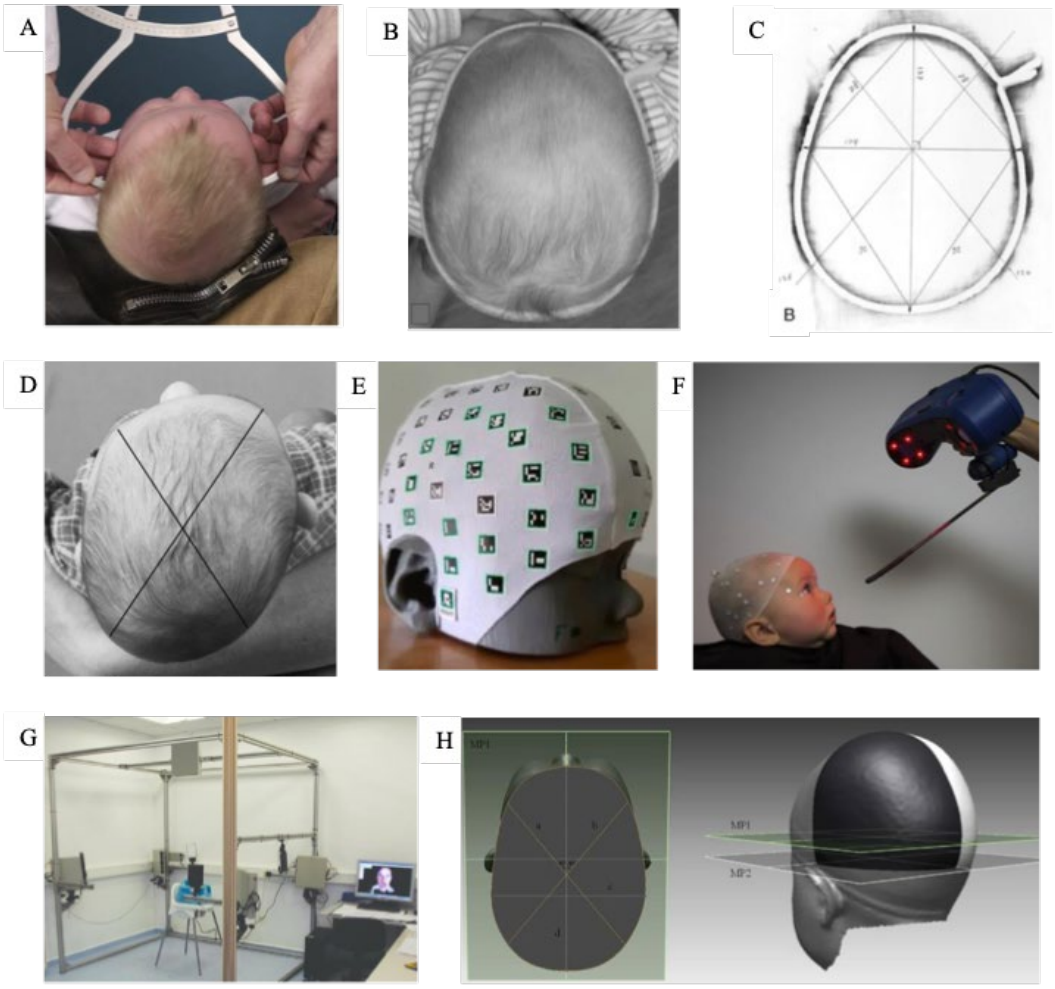
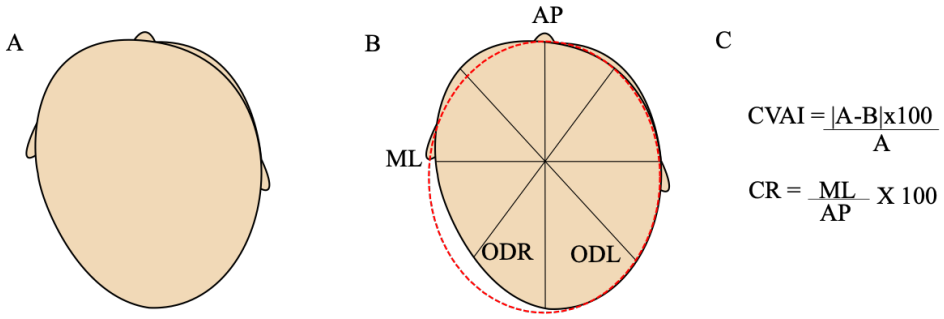


Figure 3: Processing pathway for automated digital photography measurement. (A) Top view of an infant's head affected by positional plagiocephaly. (B) Overlay of a healthy head shape (dotted line) with digitally rendered cranial measurements used to calculate standard asymmetry indices (C).



3.10 – List of Tables

Table 1: Summary of included studies

Modality	Author, Year	Study Design	Sample Size	Reference Standard	Findings
Anthropometry, standardized protocol	Wilbrand et al., 2011.[25]	Diagnostic validation study	*N* = 30	Expert measurement	Mean intra-observer variability <1.131mm^2, inter-observer variability <0.182mm^2. Overall 2mm measurement variance.
Anthropometry	Wu et al., 2020.[12]	Retrospective diagnostic validation study	*N* = 89	Computed Tomography	No statistical difference between caliper measurements and CT ($P > 0.05$) . Anterior-Posterior caliper dimensions were within 1cm of CT in 73% of cases, while 88% of transverse measurements were within 1cm of CT.
Digital Photography/Machine Learning	Callejas Pastor et al., 2020.[19]	Retrospective diagnostic validation study	*N* = 80	3D-Cranial Scanning	86.7% classification accuracy for brachycephaly and plagiocephaly. Cephalic ratio and cranial vault asymmetry index correlation coefficients were 0.85 and 0.89 respectively.
Digital Photography	Schaaf H et al., 2010.[26]	Diagnostic validation study	*N* = 122	Anthropometry	Cephalic index cranial vault asymmetry index intraclass correlation coefficients were 0.982 and 0.946, respectively. Digital photography satisfied the limits of agreement (cephalic index, 7.51%; cranial vault asymmetry index, 6.57%)
Digital Photography	Lopes Alho et al., 2020.[16]	Diagnostic validation study (case control)	*N* = 2	None	SymMetric can differentiate between control and plagiocephalic patients in the superior view and detected clinical improvement following orthotic use.
Digital Photography/ Machine Learning	Agarwal et al., 2018.[20]	Diagnostic validation study (augmented database)	*N* = 1006 images (75:25 Training:Test distribution)	Professionally Classified Images	AUC of 0.95 for cleft abnormality and craniosynostosis. Validation accuracy of model is 92.22%, testing accuracy is 84.12%.
Digital Photography/ Machine Learning	Bookland et al., 2021.[27]	Retrospective diagnostic validation study	*N* = 339 retrospectively collected cranial images, 40 open-source cranial images.	Professionally Classified Images/ Optical Scan Derived Craniometric Measurements	Cranial shape classification had an accuracy of 93.3% (95% CI 86.8-98.8; $p < 0.001$), with a sensitivity of 92% and a specificity of 94.3%. Intraclass correlation coefficients for measurements of the cephalic index and cranial vault asymmetry index compared to optical measurements were 0.95 (95% CI 0.84–0.98; $p < 0.001$) and 0.67 (95% CI 0.24–0.88; $p = 0.003$).
Digital Photography/ Machine Learning	Geisler et al., 2021.[28]	Diagnostic validation study	*N* = 1076 images	Professionally Classified Images	ResNet-50 CNN obtained an overall accuracy of 90.6% for diagnosing craniosynostosis. Sensitivity and precision for a combined top-front view were 100% and 100% for metopic synostosis, 93.3% and 100% for sagittal synostosis, 66.7% and 100% for unicoronal synostosis.

Digital Photography	Hutchison et al., 2005.[21]	Diagnostic validation study (case control)	*N* = 31	Flexicurve ruler	Oblique Cranial Length Ratio >106% can define plagiocephaly, Cephalic Index > 93% can define brachycephaly. Photographic method was better tolerated by infants, more repeatable, and preferred by mothers.
Plagiocephalometry	van Adrichem et al., 2008.[13]	Diagnostic validation study	*N* = 21	3D-Computed Tomography	No statistical difference ($P > 0.05$) between plagiocephalometry ring (removed from the head) and CT-based skull measurements.
3D Laser Scanning	Nahles et al., 2018.[15]	Diagnostic validation study	*N* = 44	Anthropometry	Mean head circumference was 441.5 mm for the anthropometric measurements and 441.6 mm for the laser scan method, with no significant difference between the two methods. A significant difference was found regarding the head width ($p < 0.001$), head length ($p < 0.05$), diagonals ($p < 0.001$), and distance ex-t ($p < 0.001$). Mean scan time for scanning was 579.6s in contrast to 180.5s for the manual anthropometric method.
3D Photography	Aarnivala et al., 2017.[6]	Diagnostic validation study	*N* = 407 images	Expert rating with Argenta classification	Oblique cranial length ratio consistently provided the best discrimination in terms of 3D imaging area under the curve values. Optimal cut-off values for deformational plagiocephaly (Argenta class ≥ 1) across all age-groups were 104.0% for oblique cranial length ratio (83% sensitivity, 97% specificity), 10.5% for posterior cranial asymmetry index (90% sensitivity, 90% specificity), and 24.5 for weighted Asymmetry Score (88% sensitivity, 90% specificity).
3D Photography	Schaaf et al., 2010.[7]	Retrospective diagnostic validation study	*N* = 100	Anthropometry	Comparison of the 3D photographic and callipers measurements showed that 3D photography resulted in a slight over-estimation. Inter-rater reliability was 0.97 for plagiocephaly and 0.98 for brachycephaly.
3D Photography	Skolnick et al., 2014.[8]	Retrospective Diagnostic validation study	*N* = 26	Non-linear measures from 3D photographs	The linear measure that best correlated with the inclusive measures of asymmetry was FZ-EU, the distance from the frontozygomaticus to the contralateral eurion ($r \geq 0.90$). Correlations between measures ($0.10 < r < 0.95$) and intrarater reliability (correlation coefficients from 0.42 to 0.99) of linear measurements varied widely.
3D Photography/Machine Learning	Porras et al., 2019.[22]	Retrospective Diagnostic validation study	*N* = Train: 201, Test:18	Computed Tomography	The algorithm detected craniosynostosis automatically with 94.74 percent sensitivity and 96.02 percent specificity. It further correctly identified the fused sutures with 99.51 percent sensitivity and 99.13 percent specificity.
3D Photography/Machine Learning	de Jong et al., 2020.[23]	Retrospective Diagnostic validation study	*N* = 213	Computed Tomography	195 out of 196 3D stereophotographs (99.5%) were correctly classified for a craniosynostosis diagnosis by the deep learning algorithm.
3D Photography	Barbero-García et al., 2020.[11]	Retrospective Diagnostic validation study	*N* = 5	Computed Tomography / Magnetic Resonance Imaging	CT/MRI confirmed accuracy below 1.5 mm. Basic automatically derived anthropometric linear magnitudes obtained a mean variability of 0.6 ± 0.6 mm for the longitudinal and transversal distances and 1.4 ± 1.3 mm for the maximum perimeter

3D Photography	Barbero-García et al., 2018.[18]	Diagnostic validation study	*N* = 10	Computed Tomography / Magnetic Resonance Imaging	Smartphone based 3D photogrammetric models overestimated measurements by up to 3.2 mm due to both hair and usage of caps. Differences in shape are below 1.5 mm for every patient.
3D Photography/Machine Learning	Barbero-García et al., 2021.[14]	Diagnostic validation study	*N* = 5	Target based coded markers on a cap	Precision of cap points in the generated 3D point cloud is close to 1 mm. Eye detection returned a standard deviation around 2mm; mouth and nose detection had standard deviations of 8.1 and 5.7 mm respectively.
3D Photography	Meulstee et al., 2017.[9]	Diagnostic validation study	*N* = 100	Computed Tomography	Principal component analysis was used to find the mean cranial shape and the cranial shape variation in the normal population. The model distinguished scaphocephaly ($p < 0.001$) and trigonocephaly ($p > 0.001$) patients from the normal population.
3D Photography/Machine Learning	Tu et al., 2019.[24]	Diagnostic validation study	*N* = 28	Computed Tomography	The trained support vector machine classifier obtained an improved accuracy of 91.03% in the detection of craniosynostosis, compared to 78.21% obtained using head circumference or cephalic index.
3D Photography	Atmosukarto et al., 2010.[10]	Diagnostic validation study	*N* = 254	Expert Rating	Novel 3-D-based plagiocephaly posterior severity scores provided better sensitivity and specificity in the discrimination of plagiocephalic and typical head shapes than the 2-D measurements provided by a close approximation of oblique cranial length ratio. AUC statistics were as follows: Left Posterior Flattening Score (97%), Right Posterior Flattening Score (91%), Asymmetry Score (99%), Absolute Asymmetry Score (91%) and approximation of a previously described 2-D measure, the Oblique Cranial Length Ratio (79%).

Table 2: Summary of included modalities

Modality	Summary	Advantages	Disadvantages	Comparable to Gold Standard (3D-CT)	Clinical Availability

Anthropometry	Anthropometry uses calipers and measuring tapes to take assorted measurements of the child's head. These measurements are then used to calculate cranial asymmetry indices (CVAI, CI, OCLR, etc.)	-Simple -Rapid -Quantitative -Low cost -<2mm inter/intrarater variability with standardized protocol	-Requires calipers -Subjective landmark identification -2D (cannot measure diagonal and vertical cranial dimensions) -Requires standard protocol for good reliability	Yes, no statistically significant differences	Currently Available
Plagiocephalometry	Plagiocephalometry uses a thermoplastic band wrapped around the child's head to make a mold that can be traced onto a paper. This trace can then be used to take measurements and calculate asymmetry indices without the child moving around.	-Acceptable inter/intrarater reliability -Low cost -Mean difference between CT and plagiocephalometry <1 mm.	-Requires thermoplastic band and tracing -Subjective landmark identification -2D (cannot measure diagonal and vertical cranial dimensions) -More time-consuming than anthropometry	Yes, no statistically significant differences	Currently Available

Digital Photography	Most commonly a digital photograph will be taken from the birds-eye-view perspective of the child's head. Measurements can then be taken directly off the photo with manual landmark selection. Automated methods also exist that take a photo as input and return a diagnosis using automatically calculated asymmetry indices.	-Rapid -Reproducible -Low variation -Can use smartphone to take photo -Can leverage AI for automated measurement and analysis of photos -Photos can be reviewed at a later date for comparison -Not affected by patient age	-Manual landmark selection is subjective -Automatic methods need larger training datasets to increase accuracy -2D (cannot measure diagonal and vertical cranial dimensions) -Artificial intelligence based systems are limited by training data availability	N/A	Yes, but portable smartphone-based tools require further refinement.
3D Photogrammetry	3D photogrammetry uses multi-camera stationary imaging setups or, more recently, the slow-motion features on modern smartphones. A 3D image is pieced together from a large number of still photos taken from different perspectives. Multi-camera setups typically require the child be fitted with a nylon cap. Cranial asymmetry can be evaluated using 2D anthropometric indices or more complicated 3D indices.	-3D Representation of the head -Rapid -Smartphone based methods are cheap - Can leverage artificial intelligence for automated measurement and analysis of head shape -Can correctly identify the fused suture in craniosynostosis -Multi-camera installations are immune to infant movement (<1s acquisition time) -Not affected by patient age	-Typically requires a nylon cap -Multi-camera installations are expensive, require a dedicated room and expert operation -Some smartphone-based methods can be susceptible to patient movement -Artificial intelligence-based systems are limited by training data availability	Yes, no statistically significant differences	Yes, but limited to specialized centers (not accessible to pediatricians)

3D Laser Scanning	3D Laser scanning uses a stationary or handheld scanner to create a 3D representation of the infant's head. The infant must be fitted with a nylon cap with reflective dots. 2D anthropometric or more complex 3D indices can be used to determine cranial asymmetry.	- 3D representation of the head - No advantages compared to anthropometric measurement when using 2D indices	-Requires dot fixation with a nylon cap for 3D scanning -Significantly longer than anthropometric methods -High acquisition, service and maintenance cost -Inconsistent results	N/A	Yes, but limited to specialized centers (not accessible to pediatricians)

Table 3: Risk of bias assessment using QUADAS-2

Author, Year	Domain 1				Domain 2			Domain 3				Domain 4					Overall
	Q1	Q2	Q3	Result	Q1	Q2	Results	Reference Standard	Q2	Q3	Result	Q1	Q2	Q3	Q4	Result	
Wilbrand et al., 2011.[25]	Y	Y	Y	Low	Y	Y	Low	Expert measurement	Y	Y	Low	Y	Y	Y	Y	Low	Low
Wu et al., 2020.[12]	Y	Y	Y	Low	Y	Y	Low	Computed Tomography	Y	Y	Low	Y	Y	Y	Y	Low	Low
Callejas Pastor et al., 2020.[19]	U	Y	U	Unclear	Y	Y	Low	3D-Cranial Scanning	Y	Y	Low	Y	Y	Y	Y	Low	Low

Schaaf H et al., 2010.[26]	Y	Y	Y	Low	U	Y	Low	Anthropometry	Y	U	Low	Y	Y	Y	Y	Low	Low
Lopes Alho et al., 2020.[16]	N	N	U	High	N	N	High	None	N	N	High	N	N	N	Y	High	High
Agarwal et al., 2018.[20]	Y	Y	Y	Low	Y	Y	Low	Professionally Classified Images	Y	Y	Low	U	U	U	Y	Low*	Low
Bookland et al., 2021.[27]	Y	Y	Y	Low	Y	Y	Low	Professionally Classified Images/ Optical Scan Derived Craniometric Measurements	Y	Y	Low	Y	y	N	N	Low	Low
Geisler et al., 2021.[28]	Y	Y	Y	Low	Y	Y	Low	Professionally Classified Images	Y	Y	Low	Y	Y	Y	Y	Low	Low
Hutchison et al., 2005.[21]	Y	N	Y	Low	Y	Y	Low	Flexicurve ruler	Y	Y	Low	Y	Y	Y	Y	Low	Low
van Adrichem et al., 2008.[13]	Y	Y	Y	Low	Y	Y	Low	3D-Computed Tomography	Y	Y	Low	Y	Y	Y	Y	Low	Low
Nahles et al., 2018.[15]	U	Y	Y	Low	Y	Y	Low	Anthropometry	Y	Y	Low	Y	Y	Y	Y	Low	Low
Aarnivala et al., 2017.[6]	Y	Y	Y	Low	N	Y	Low	Expert rating with Argenta classification	Y	Y	Low	Y	Y	Y	Y	Low	Low
Schaaf et al., 2010.[7]	Y	Y	Y	Low	Y	Y	Low	Anthropometry	Y	Y	Low	Y	Y	Y	Y	Low	Low
Skolnick et al., 2014.[8]	U	Y	Y	Low	Y	Y	Low	Non-linear measures from 3D photographs	Y	U	Unclear	Y	Y	Y	Y	Low	Low

Porras et al., 2019.[22]	U	Y	Y	Low	Y	Y	Low	Computed Tomography	Y	Y	Low	Y	Y	Y	Y	Low	Low
de Jong et al., 2020.[23]	U	N	Y	Unclear	Y	Y	Low	Computed Tomography	Y	Y	Low	Y	N	Y	N	Low	Low
Barbero-García et al., 2020.[11]	N	N	U	High	Y	Y	Low	Computed Tomography / Magnetic Resonance Imaging	Y	Y	Low	Y	Y	N	Y	Low	High
Barbero-García et al., 2018.[18]	U	Y	Y	Low	Y	Y	Low	Computed Tomography / Magnetic Resonance Imaging	Y	Y	Low	Y	Y	N	Y	Low	Low
Barbero-García et al., 2021.[14]	N	Y	Y	Low	Y	Y	Low	Target based coded markers on a cap	U	U	High	U	U	U	Y	High	High
Meulstee et al., 2017.[9]	U	N	Y	Low	Y	Y	Low	Computed Tomography	Y	Y	Low	Y	N	Y	Y	Low	Low
Tu et al., 2019.[24]	U	N	Y	Low	Y	Y	Low	Computed Tomography	Y	Y	Low	Y	N	U	Y	Low**	Low
Atmosukarto et al., 2010.[10]	Y	N	Y	Low	Y	Y	Low	Expert Rating	Y	Y	Low	Y	Y	Y	N	Low	Low

* Machine learning database did not use "real patients"

** Healthy CT controls were used to construct a normative shape multi-atlas. It is unclear if craniosynostosis patients were CT-confirmed, but they were status pre-op.

† Y = Yes, U = Unclear, N= No

3.11 – Bridging Text

The previous systematic review comprehensively detailed the non-radiographic diagnostic imaging modalities available for positional plagiocephaly. Given the typically subjective nature of a clinical plagiocephaly diagnosis, the recent increase in quantitative modalities is promising for ensuring consistent and accurate diagnosis for infants with cranial deformities. Unfortunately, many of the included diagnostic tools reviewed above were limited by dependence on specialized centers, high cost, or long capture times. Effective implementation of a diagnostic tool in a physician's practice requires a higher degree of efficiency, ease-of-use, and lower cost barriers. Given the results of this systematic review and the trends observed in technological advancement, mobile smartphones seem poised as a strong platform to satisfy these criteria and deliver an optimized diagnostic tool to the pockets of physicians. Ultimately, the goal is to provide primary care physicians with a tool capable of quantitatively tracking head shape over time to support earlier diagnosis of positional plagiocephaly. Resultingly, as discussed in Chapter 2, we would expect improved clinical outcomes and lower costs to the family and healthcare system. The following manuscript discusses the implementation of a novel diagnostic AI algorithm on the Apple iPhone platform, and a subsequential clinical pilot study to evaluate it's efficacy in the clinical setting. The results of this study support the predictions made following analysis of the available literature and offers a glimpse at the potential smartphone integrated AI could hold when further optimized and supported by ever-improving hardware.

Chapter 4 – Smartphone Integration of Artificial Intelligence for Automated Plagiocephaly Diagnosis

4.1 – Title Page

Smartphone Integration of Artificial Intelligence for Automated Plagiocephaly Diagnosis

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4.2 - Abstract

Objective: To determine whether the prospective application of a smartphone based artificial intelligence (AI) tool could result in clinically useful diagnoses of positional plagiocephaly in a pediatric population.

Design, Setting, and Patients: This prospective validation study used a multi-site recruiting strategy to obtain a total sample size of 139 infants under 12 months of age. This sample was broken down into sub-populations based on recruitment site: either the newborn nursery of a major urban hospital (n = 107) or the outpatient craniofacial surgery clinic at a major children's hospital (n = 27). Recruitment took place between November 2021 and February 2022. Data underwent preprocessing to remove images that were substantially off angle, included significant shadows, or had objects (such as a parent's hand) on the border of the cranial contour; the final dataset was comprised of 89 images and the AI model was run on the entire dataset.

Exposures: The AI algorithm leverages a combination of automatic edge detection (segmentation by active contouring) and a pre-trained convolutional neural network (a form of machine learning) to automatically contour a birds-eye-view image of the infant's head. This contour is then used to infer anthropometric distances and calculate cranial asymmetry indices used for diagnostic purposes.

Main Outcomes and Measures: Sensitivity, specificity, accuracy, OFF-1 score, F1-score, precision, positive and negative predictive values, likelihood ratios, the diagnostic odds ratio, and the Matthew's Correlation Coefficient were used to evaluate clinical performance for the model's prediction of positional plagiocephaly.

Results: A total of 89 infants (56 males [63%], 33 females [37%], mean age 2.37 months) were prospectively enrolled in this study following the obtention of signed informed consent from a parent or guardian. Recruitment occurred at two sites: the craniofacial surgery clinic (n=25, 17 males [68%], 8 females [32%], mean age 8.44 months) and the newborn nursery (n=64, 29 males [45%], 25 females [39%], mean age 0 months. The model obtained a diagnostic accuracy of 85.39% when compared to a gold standard clinical examination. The OFF-1 score was 92.05%, with a sensitivity of 87.50% [95%cCI, 75.94-98.42] and a specificity of 83.67% [95% CI, 72.35-94.99]. The precision was 81.40%, with a positive predictive value of 81.40% and a negative predictive value of 89.13%. Likelihood ratios were 5.36 and 0.15 for the positive and negative ratio, respectively. Consequently, the diagnostic odds ratio was 35.875. The F1-score was 84.34% and the Matthew's Correlation Coefficient was 0.7047.

Conclusion and Relevance: The developed smartphone-based AI algorithm was able to accurately diagnose positional plagiocephaly in a prospective clinical environment. This technology may provide value in helping guide specialist consultation for pediatricians in the primary care setting and allows for quantitative longitudinal monitoring of cranial shape throughout development.

4.3 - Introduction

Positional plagiocephaly (or deformational plagiocephaly) is a common pediatric condition, representing a large proportion of the referrals to craniofacial clinics in recent years.[1] Since the introduction of the American Association of Pediatrics' Back to Sleep campaign in the 1990's, we have seen a dramatic reduction in sudden infant death syndrome (SIDS). However, this shift was balanced by a notable increase in the frequency of deformational plagiocephaly caused by prolonged external pressure to the back of the infant's head when put to sleep.[2-6] While this trade-off is without question the preferred option, the increase in prevalence of positional plagiocephaly to almost 40% has bolstered research efforts into long-term sequelae, neurological implications, and clinical outcomes of the diagnosis.[7, 8] Importantly, deformational plagiocephaly has been found not to imply any additional risk of neurodevelopmental deficits, presenting as a primarily aesthetic pathology with long-term psychological implications from bullying if the condition is left untreated.[9, 10]

In tangent with research into the clinical outcomes of positional plagiocephaly, researchers began looking for ways to optimize treatment protocols and facilitate earlier diagnosis. In a previous study, the authors demonstrated that earlier diagnosis is associated with better aesthetic outcomes, shorter treatment times, lower costs for treatment, a lower stress burden for parents, and lower costs for the healthcare system overall.[11] It is not surprising then that various techniques have been developed to accurately and efficiently diagnose head deformities in the pediatric population.[12] Although a number of studies have reported strong diagnostic performances for their respective tools, the majority were plagued by design limitations requiring centralization at specialized centers or high cost barriers, both of which inhibit widespread adoption and consequential amelioration of diagnosis at the point of care

(typically an outpatient visit with a child's pediatrician).[12] Given the current gold standard for diagnosis of deformational plagiocephaly remains visual assessment of the cranial form, AI systems present a promising method for objectively quantifying a previously subjective qualitative diagnosis. In turn, such a companion tool may provide physicians the necessary means (or modality) to make more informed clinical decisions.

In consideration of this context, the objective of this study was to conduct the first larger-scale prospective study of a newly developed AI tool that allows the quantitative evaluation and diagnosis of an infant's cranium, and to compare these AI-sourced diagnoses to a gold standard clinical evaluator (an experienced pediatric craniofacial surgeon).

Methods

Study Design and Patient Population

This study was approved by the appropriate institutional review board (McGill University Health Center IRB 2021-6964). A total of 139 infants between the ages of 0-12 months were prospectively recruited from two sites, either the newborn nursery of a major urban hospital (n = 107) or the outpatient craniofacial surgery clinic at a major children's hospital (n = 27), between November 2021 and February 2022. Exclusion criteria for the study included infants presenting with hydrocephalus, intracranial tumors, intra-cranial hemorrhage, hardware (e.g., shunts), or prior craniofacial surgery.

This study was conducted in accordance with applicable legislation and the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2018), as well as in respect of the requirements set out in the applicable standard operation procedures of the research institute and the recommendations of the institutional ethics committee.

Data Acquisition and Analysis

At the time of recruitment, a single 3-second video of the infants' head taken from a top-down perspective was recorded for all subjects, along with their age and sex. Additionally, a clinical evaluation of head shape and relevant clinical history was recorded as perceived by the physician of record (one of several participating pediatricians in the nursery, and a pediatric craniofacial surgeon (M.G.) at the out-patient craniofacial clinic). The time required to use the application (from initial patient data entry to completion and submission of video) was also noted during data collection. Due to the significant differences in development between newborn (<48 hours) and older (3-12 months) infants, the study implemented distinct imaging protocols for each recruitment site. Infants being seen in the outpatient clinic were required to sit on their patients' laps, looking straight ahead. In contrast, infants recruited in the nursery (typically <48 hours postpartum) were imaged cradled in their parent's arms, with the infant's head extending past the parent's elbow. Parents or medical colleagues often assisted by attracting the child's attention to minimize movement during the recording. Given the nature of the algorithm being evaluated by this study, videos were retrospectively reviewed to ensure adequate lighting, a well-centered head looking forward, and the absence of similarly coloured and/or textured objects against the contour of the infant's head. As seen in Supplemental Figure 1, poor lighting and background conflicts had significant deleterious effects on the ability of the algorithm to evaluate the head shape appropriately. Thus, the dataset underwent a thorough data preprocessing stage where images that did not meet the aforementioned criteria were removed. This was particularly relevant for infants recruited from the nursery, as the environment tended to be much darker, with varied lighting and significant shadows compared to the consistent overhead lighting in the outpatient clinic setting.

All remaining video recordings from subjects recruited in the nursery were reviewed retrospectively by an expert pediatric craniofacial surgeon (M.G.) to obtain a gold standard clinical diagnosis for all recordings in the dataset.

Measurement Algorithm

All video recordings were performed by a single member of the study team (A.W.) using an iPhone 7 Plus through a proprietary mobile application. The mobile application digitally overlays a standardised head outline over the phone's camera input to help standardise the recorded videos (Figure 1). Once recorded, the short videos and all other clinical data were automatically encrypted and sent remotely to a cloud-based server. Following data collection, the short videos were manually screened using Premiere Pro (Adobe INC., CA, USA) to identify the most representative, clear, centered frame of the head possible. This still image was then uploaded to the server for processing and analysis by the AI algorithm (Little Angel Medical Inc., QC, Canada). The AI algorithm leverages a combination of automatic edge detection (segmentation by active contouring) and a pre-trained convolutional neural network (a form of machine learning) to contour the infant's head automatically (Figure 2).

Results

Demographics

A total of 89 infants (56 males [63%], 33 females [37%], mean age 2.37 months) were prospectively enrolled in this study following the obtention of signed informed consent from a parent or guardian. Recruitment occurred at two sites: the craniofacial surgery clinic (n=25, 17 males [68%], 8 females [32%], mean age 8.44 months) and the newborn nursery (n=64, 29 males [45%], 25 females [39%], mean age 0 months. From the craniofacial clinic recruitment site, 23

patients were clinically diagnosed as having a form of positional plagiocephaly. The newborn nursery recruitment site yielded 17 patients that were retrospectively labelled by an experienced craniofacial surgeon as having positional plagiocephaly. The rest of the sample population (n=49) presented with clinically normal head shapes.

AI Output

The AI algorithm, applied to the complete dataset, correctly classified positional plagiocephaly with an accuracy of 85.39% when compared to a gold standard clinical examination. The OFF-1 score was 92.05%, with a sensitivity of 87.50% [95% CI, 75.94-98.42] and a specificity of 83.67% [95% CI, 72.35-94.99]. The precision was 81.40%, with a positive predictive value of 81.40% and a negative predictive value of 89.13%. Likelihood ratios were 5.36 and 0.15 for the positive and negative ratio, respectively. Consequently, the diagnostic odds ratio was 35.875. The F1-score was 84.34% and the Matthew's Correlation Coefficient was 0.7047. Time required to implement the application in each clinical interaction (equal across both recruitment sites) was ∼2 minutes.

Craniofacial clinic

Although representing a smaller sample size (n=25), the data obtained from patient recruitment at the pediatric craniofacial surgery clinic forms this study's best (most representative) data set. Ages ranged from 1 month to 10 months, with a median age of 6.98 months. Within this subgroup, AI performance increased measurably; OFF-1 was calculated to be 93.75% and sensitivity and specificity were 95.65% [95% CI, 87.32-103.99] and 100.00%

[95% CI, 100-100] respectively. The F1-score was 0.9778 and the Mathew's Correlation Coefficient was 0.7985.

Newborn Nursery

The nursery subset of our dataset required pre-processing due to the poor environmental conditions and young age of the children. As a result, the newborn nursery dataset was comprised of 64 images. All infants were <48 hours old at the time of imaging, and many had not yet received full baths removing vernix caseosa/amniotic fluid from the child's head. OFF-1 was calculated to be 90.63% with sensitivity and specificity returning at 76.47% [95% CI, 56.31-96.63] and 82.98% [95% CI, 72.23-93.72] respectively. The F1-score was 0.6842 and the Matthew's Correlation Coefficient was 0.5592.

Discussion

The purpose of this study was to determine whether the implementation of a smartphone-based artificial intelligence (AI) tool could result in clinically useful diagnoses of positional plagiocephaly in a pediatric population. The resultant prospective validation study of an AI-based mobile diagnostic tool obtained a sample size of 89 patients and achieved a diagnostic accuracy of 85.39%, with a sensitivity of 87.50% [95% CI: 75.94-98.42] and a specificity of 83.67% [95% CI: 72.35-94.99]. In addition to accurate diagnosis of positional plagiocephaly, the application is easy to use and takes very little time to deploy in the clinical setting (<2 min/patient).

This work follows in the footsteps of previous studies implementing a variety of digital photography and/or AI-based tools for the diagnosis of pediatric deformities. Callejas Pastor et al

published a recent study using machine learning to diagnose positional plagiocephaly from 2D images with an accuracy of 86.7%.[13] Likewise, Agarwal et al, Bookland et al, and Geisler et al (among others) published studies evaluating AI algorithms applied to 2D digital photographic images, with testing accuracies for synostotic deformities of 84.12%, 93.3%, and 90.6% respectively.[14-16] Importantly, however, all of the implementations above were trained and/or evaluated on a retrospectively curated dataset and were run on a desktop computer, limiting the translation of results to the primary care environment. Furthermore, there exists intrinsic biases that are present in AI systems applied to retrospective datasets. Most importantly, the Clever-Hans type bias suggests that machine learning models may make predictions on spurious correlations in training data that do not exist in the real world, a significant barrier in the translation from pre-clinical to clinical (real world) diagnostic performance.[17-19] Our results represent the diagnostic outcomes of an AI tool deployed prospectively, avoiding the Clever-Hans bias entirely. This is particularly relevant considering that our clinical accuracy was in line with previous studies' pre-clinical findings.[14-16]

Despite the inherent validation advantages of conducting a prospective study, there are notable challenges to be addressed. In this study, the authors faced significant difficulty deploying the AI tool in the newborn nursery thanks to contextual and environmental factors, leading to a substantial loss of data (~40%). Given the delicate nature of recruiting families for participation in a study within 24-48 hours of a child's birth, certain accommodations were made. The most prominent was capturing head photos with poor and/or indirect lighting, which led to substantial shadows in the image and consequential poor AI performance (Supplemental Figure 1). Furthermore, infants had often not received their first bath yet, meaning that heads were often covered in vernix caseosa/amniotic fluid which created abnormal edges within the contour of the

skull. These challenges led us to conduct a thorough data pre-processing where images with significant shadows, poor lighting, etc. were excluded to better evaluate the performance of the AI tool. As a counterbalance to the poor conditions found in the newborn nursery, we performed a subgroup analysis to evaluate AI performance in both clinical environments (newborn nursery + craniofacial clinic). The craniofacial clinic subgroup is formed of a more representative population for plagiocephaly diagnosis (age range 1-10 months, median age 6.98 months) and was much better controlled for lighting and environment, albeit with a much smaller sample size (n=25). Consequentially, the craniofacial clinic subgroup saw substantially stronger AI performance. Given the dichotomy between the two subgroups in infant age and environmental conditions for photography, the authors consider the overall AI accuracy of accuracy of 85.39%, representing performance in both sub-optimal and well controlled conditions to be a reasonable prediction of diagnostic strength.

Evaluation of any diagnostic tool is dependent on comparison to a reliable gold standard which informs diagnostic performance. In this study, the AI tool was compared to the clinical judgment of an experience pediatric craniofacial surgeon (M.G.). Clinical diagnosis is broadly recognized in the field as the standard diagnostic modality for positional plagiocephaly; although radiographic options (such as CT) offer quantitative evaluation of head shape, they require exposure to radiation and/or anesthesia in a vulnerable population and are typically reserved for evaluation of a potential craniosynostosis.[20-27] The method for assignment of the gold standard diagnosis in the study was subgroup dependent. In the craniofacial clinic setting, patients were directly evaluated and a clinical decision was recorded by an experience craniofacial surgeon prior to capturing an image of the child's head. This value was then compared to the AI result.

The AI tool described in this study has several potential applications in the healthcare pathway. Given high patient volumes and short appointment times, pediatricians are faced with a significant challenge when monitoring infantile head shapes with no way to evaluate progression over time.[28] A significant advantage of an algorithmic approach to diagnosis in the primary care setting is the ability to longitudinally track development in head shape beyond the head circumference, a common part of growth monitoring in infants. This promotes an ability to identify subtle trends in cranial development and can inform the need to refer for specialist consultation and management.

Additionally, handheld, easy-to-use diagnostic tools have a place in both parental monitoring and telemedicine applications. Parents play an essential role in the initial identification of positional plagiocephaly, often identifying cranial asymmetry and bringing it to the attention of the infant's pediatrician.[11] In this capacity, smart diagnostic applications that do not require specialized training have the potential to be powerful community-level screening tools. A longitudinal record of head development, recorded by parents, could help guide clinical decision-making for the treating physician. A demonstrated negative trend, for instance, could be indicative of a potential synostotic deformity, requiring consultation with pediatric craniofacial and/or neurosurgical teams. Conversely, a positive trend in cranial symmetry following at-home implementation of additional tummy time and physiotherapy may indicate a resolving plagiocephaly requiring monitoring but no additional consultation.[11, 28]

Recent events have highlighted an urgent need for improved modalities to provide adequate care remotely with telemedicine.[29, 30] Rizvi et al, alongside Marianayagam et al, have released studies evaluating the outcomes of virtual craniofacial clinics for the assessment of positional plagiocephaly based on standard digital images; both concluded that the virtual encounters

resulted in comparable diagnostic accuracy.[29, 30] Implementation of an AI tool similar to the one described in this study would further enhance that interaction by providing quantifiable metrics that treating physicians could use to support a clinical diagnosis. Outside of the context of a global health crisis, targeted improvement of telemedicine capability allows providers to deliver high-quality care to rural and small populations, a subset of patients that has historically been neglected.[31]

Finally, the implementation of easy-to-use AI tools in the clinical environment gains importance in the context of longitudinal monitoring for suspected or confirmed cases of synostotic plagiocephaly, particularly in cases of single-suture fusion where surgical intervention is either a) not indicated or b) delayed with continuous monitoring to optimize perioperative safety.[32] In these cases, the gold standard for clinical diagnosis is high-resolution 3D computed tomography (3D-CT). Given the resulting movement to radiation and anesthesia stewardship in pediatric populations, implementing a non-radiographic modality without anesthesia in infants to longitudinally monitor head development (alongside serial ophthalmologic exams) could be a valuable tool in the pocket of pediatricians and consulting specialists alike. Pathological changes in the growth pattern of the cranium could serve as an indication for follow-up and potential evaluation by 3DCT.[33]

Limitations

Despite the promising results obtained from the smartphone-integrated AI algorithm in question, the prospective study methodology employed has limitations. Firstly, although being the largest of its kind in the literature, our sample size remains small for the validation of an AI tool; this result can be seen in the large spread of the 95% CI for the sensitivity and specificity

metrics. Second, images obtained during recruitment at the newborn nursery imposed substantial challenges due to the infants' age and environmental context, as previously discussed. Consequently, we were forced to discard 40% of those images. Conversely, the craniofacial clinic (containing a more representative population and a much better controlled environment) only required discarding of two images due to sudden movement of the infant during the video that left the resulting still image significantly off-angle and therefore not representative of the cranial outline. Third, all data was captured by a single member of the study team (A.W.) with a single capture of each infant's cranium, removing our ability to run intra- and inter-rater reliability analyses.

Conclusion

This study demonstrates the convincing performance of a smartphone-based AI-enabled diagnostic tool in one of the largest prospective validation studies in the craniofacial literature. The implementation of a tool as described in this study would give pediatricians and parents the ability to quantitatively, non-invasively, affordably, and crucially, without radiation, monitor the development of a child's head both at the point of care and longitudinally throughout the child's development. Such an implementation would simultaneously assist primary care givers in obtaining objective head shape measures and, importantly, to promote early diagnosis and treatment of positional plagiocephaly which have been shown to improve outcomes and lower costs.

4.9 - References

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4.10 – List of Figures

Figure 1: Digital overlay of cranial outline to standardize and guide video recordings.

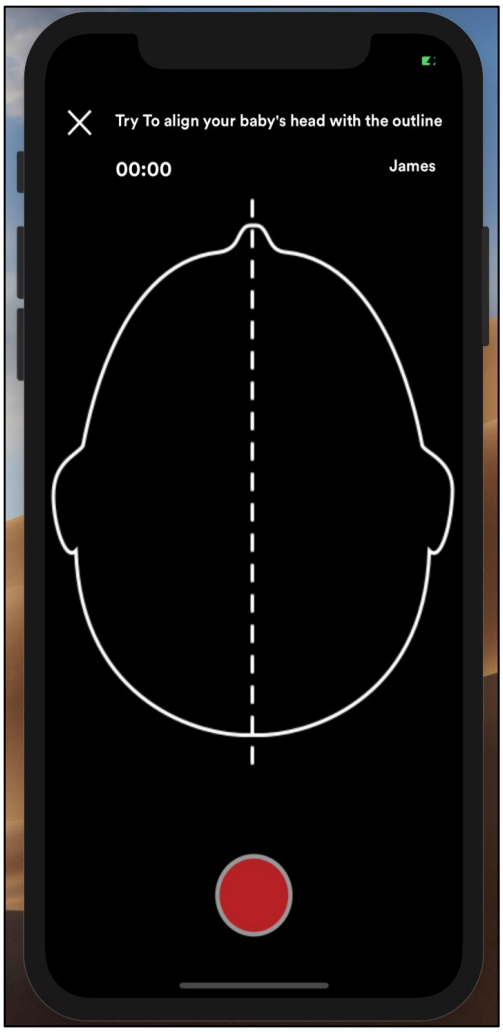


Figure 2: Infants head before (A) and after (B) automatic AI contouring of the cranium with defined cranial measurements (AP, ML, ODL, ODR) which are subsequently used to calculate craniometric indices for diagnostic purposes (C).

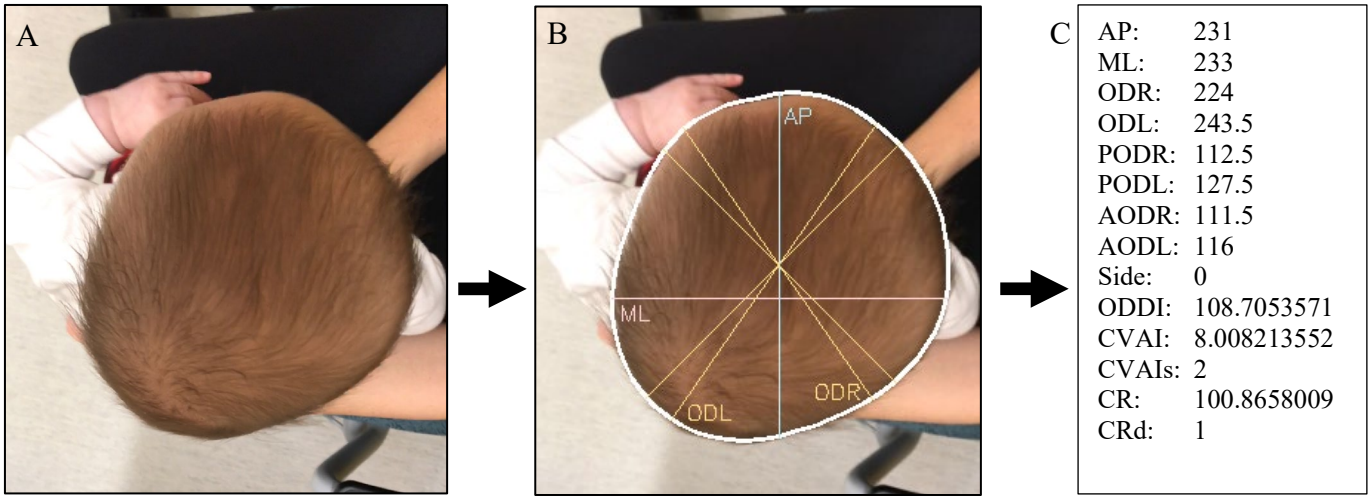
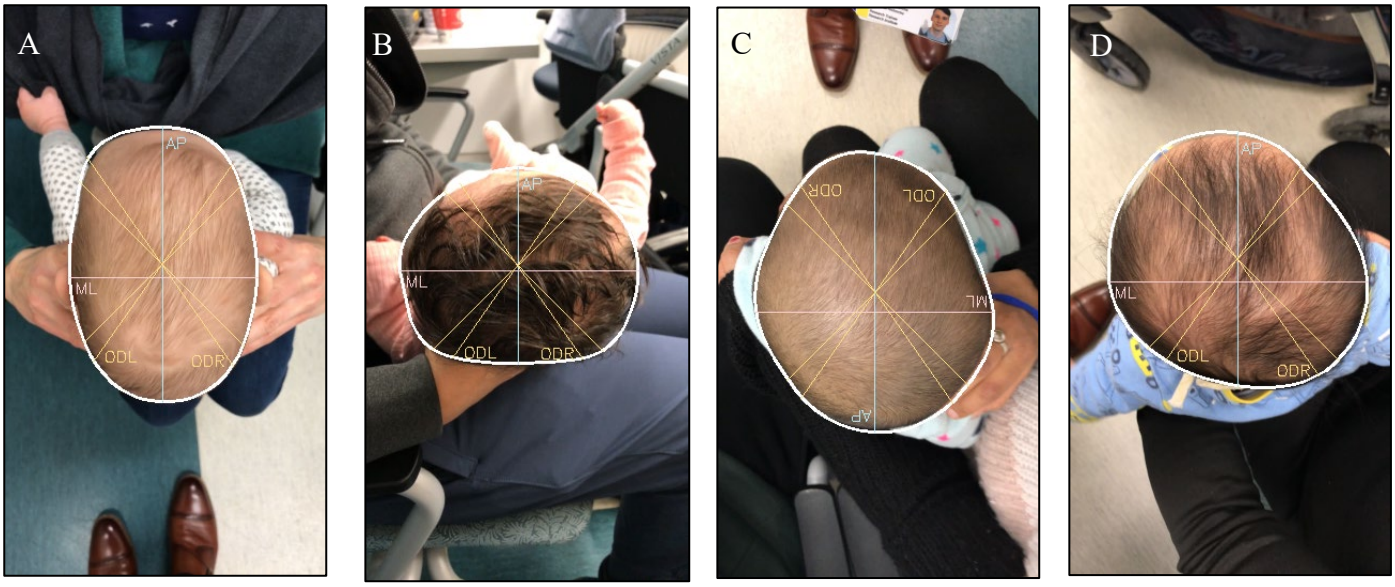
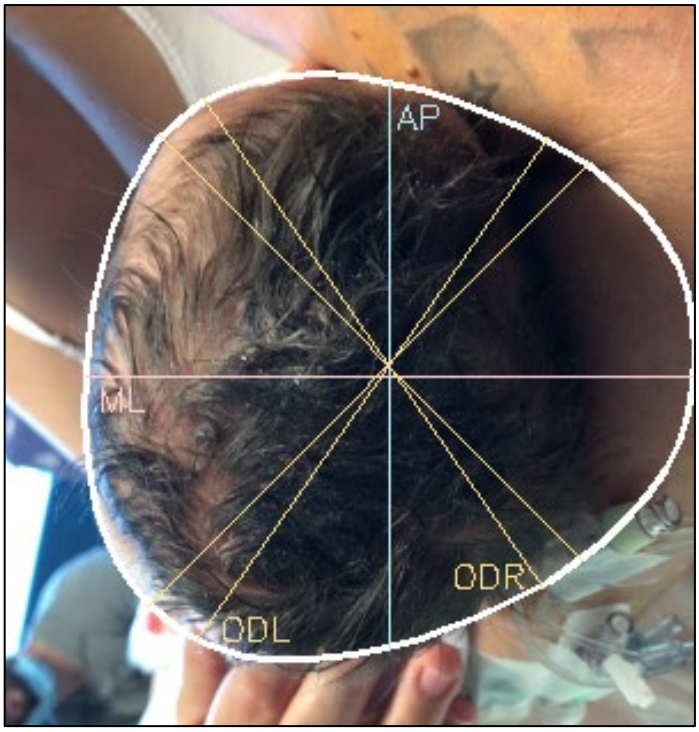


Figure 3: Automatically applied AI contour is capable of contouring a broad range of head shapes: (A) Moderate scaphocephaly, (B) Bilateral coronal synostosis (severe brachycephaly), (C) Moderate left positional plagiocephaly, (D) Severe left positional plagiocephaly.



Supplemental Figure 1: Data collected from the Newborn Nursery was often poorly illuminated with background conflicts, increasing the difficulty of obtaining an accurate cranial contour.



5 – Discussion and Future Directions

This thesis aimed to evaluate a novel diagnostic tool for pediatric cranial deformity and explore the use case for integration of similar technologies at the point of care. Further, we evaluate the breadth of currently available tools and modalities which form the competitive landscape for assisted diagnosis of positional plagiocephaly.

Understanding the "why" of a problem is an important part of justifying research, particularly in the medical field where ethics committees rigorously evaluate clinical research to ensure our work provides value to the community. Financial and quality-of-life implications are relevant parts of a medical diagnosis, which gain further importance in pediatric subspecialties where both the patient and their parent's/guardians carry the burden of disease, whether it be directly or indirectly. Previously, very little had been done to look beyond the obvious clinical implications and elucidate the importance of timely diagnosis in positional plagiocephaly. Thus, to understand the entire scope of why appropriate and timely identification of positional plagiocephaly is important, we comprehensively evaluated the available literature and reported on the findings.

To begin, we simulated treatment programs that stemmed from landmark publications to simulate financial burdens associated with position plagiocephaly; the resultant calculations informed us of a significant discrepancy in cost that was dependent on a patient's age at the time of diagnosis and the severity of their condition; early diagnosis yielded a cost less than 1/3 that of a diagnosis occurring two months later ($1,495 vs $5,195). Similar discrepancies were noted when evaluating the stress burden on parents, typically relating to financial concerns, time lost to travel, and social conflicts. Concurrently, we demonstrated that earlier diagnosis unequivocally leads to improved clinical outcomes in children diagnosed with positional plagiocephaly.

Effectively, these results support the economic, moral, and clinical viability of diagnostic tools that can promote earlier diagnosis at the community level.

Once we had a broad understanding of the case for supporting early identification of positional plagiocephaly, we sought to evaluate the current state-of-the-art with regards to available diagnostic modalities. Notably, this search excluded all radiographic or otherwise invasive diagnostic modalities. Though 3D-CT or Black Bone MRI are understood to provide the absolute best views potential cranial deformities, these modalities require subjecting infants to either a) radiation or b) general anesthesia. Given current efforts with regards to pediatric radiation and anesthesia stewardship, we focused on those modalities that were completely non-invasive. A broad systematic review followed, which highlighted 5 unique modalities that aimed to enhance physician evaluation or provide automated diagnostics: anthropometry, plagiocephalometry, digital photography, 3D laser scanning, and 2D photogrammetry.

Simple visual assessment is well documented in practise and the literature as the most common method of evaluating for cranial asymmetry. The outcomes of the systematic review enforced that there is a growing list of quantitative diagnostic modalities equivalently capable of monitoring head shape that are becoming available to physicians. Of mention was the substantial increase in recent years of publications that relate to artificial intelligence (AI)-based tools. The strong diagnostic performance achieved by these models (typically in the 80-90% accuracy range) serves as a promising testament to the power of AI tools applied specifically to cranial deformity analysis.[8-11]

Viable diagnostic tools need to meet several criteria to achieve real success in the clinical environment. Although the aforementioned AI tools achieved strong preclinical results, they were all tied to slow implementations and typically were reliant on purpose-built desktop

computers to run the AI model. This limits the ability to effectively translate results to the clinical environment by reducing the diagnostic efficiency and economic viability of the solution. In addition, previous studies used retrospective study methods, which forces readers to take results with a grain of salt when considering the implementation of a diagnostic modality that will be subject to the challenges provided by hyperactive children, real world lighting conditions and end-user variability.

With a solid grasp of the clinical need, the landscape of current diagnostic solutions, the trend towards AI implementation and an understanding of common methodological and solution-based shortcomings, we turned our attention to evaluating a novel AI-based diagnostic tool that had been ported to the apple iOS platform for use in smartphones.

A multi-site clinical validation study utilizing a prospective recruitment methodology followed, recruiting a total of 139 infants; this represented the largest such study in the field at the time of writing. The model obtained a diagnostic accuracy of 85.39% when compared to a gold standard clinical examination. The OFF-1 score was 92.05%, with a sensitivity of 87.50% [95%cCI, 75.94-98.42] and a specificity of 83.67% [95% CI, 72.35-94.99]. The precision was 81.40%, with a positive predictive value of 81.40% and a negative predictive value of 89.13%. Likelihood ratios were 5.36 and 0.15 for the positive and negative ratio, respectively, leading to a diagnostic odds ratio was 35.875. The F1-score was 84.34% and the Matthew's Correlation Coefficient was 0.7047. These results correspond to an overall strong diagnostic ability of the smartphone-based AI algorithm. Outcomes were comparable to the results obtained by previous studies using retrospective evaluation methods, which serves as a promising point of reference for the placement of our model in the rank list of available diagnostic tools.

The results obtained in our prospective validation study are not without limitation, however. Stemming from both the AI software implementation and the study protocol, notable limitations that impact our outlook of clinical results include the manual frame selection and heavy bias of data towards newborn infants. Use of manual frame selection removed possible error while evaluating the performance of the AI algorithm itself, but due consideration should be given to potential performance reductions when an automatic system is implemented. The sample population captured in Chapter 4, composed majoritarily of newborn infants, represents the greatest limitation of this Thesis. Given that most children that present with positional plagiocephaly find themselves between 3-12 months of age, the unique imaging challenges faced in the newborn nursery are not representative of a real-life application of the AI software being evaluated. Fortunately, we were able to compare these results to those collected in the craniofacial surgery clinic, which formed a much more representative (albeit smaller) database. This comparison suggested that AI performance in the craniofacial clinic (which we postulate is the closest to real-world data) was greater than in the Nursery subgroup. Therefore, we assume that although the Nursery dataset was a significant limitation in the design of the study, it's effect on the outcomes was negative, and there was no resulting artificial inflation of AI performance.

As previously mentioned, there exists substantial benefits to achieving earlier diagnosis of positional plagiocephaly in infants. Unfortunately, this is not a trivial goal. Meaningful reductions in average age at the time of diagnosis requires improvement of the standard of care at the community level, whether that be pediatricians or family physicians. Due to high patient volumes and short appointment times, useful clinical tools need to be efficient to use, provide real improvements in diagnostic ability, and be cost effective. As stated previously, many of the

modalities expanded on with our systematic fail to meet at least one of these criteria, limiting their translatability to clinical practice. Conversely, the AI tool that we evaluate in this Thesis takes very little time to use (<2 min), provides a method to longitudinally monitor cranial growth and directly compare head shape evolution both visually and quantitatively. Furthermore, it makes use of a modality all physicians already have in their back pocket (the smartphone), significantly lowering any costs associated with the adoption of the tool into the clinic.

True validation of medical devices requires large scale studies that are beyond the scope of this thesis. Nonetheless, the work described here lays a solid foundation for further development of this, and other, diagnostic tools. Continued work towards advancing automation will prove to be particularly valuable as we move forward with AI tools in the medical field. Current solutions, including the AI model evaluated in this work, depend on a degree of human intervention. In our case, we filmed short videos of the infants head and manually selected the most representative frames for analysis by the algorithm; this was done to avoid blurring or image quality/content issues that may have arisen from the movement of infants during image capture. Manual image adjustment is a common occurrence in similar AI-based studies. De Jong et al, who published a landmark study using 3D photogrammetry and deep learning to diagnose varying types of craniosynostosis with 100% sensitivity and specificity, also manually positioned their images using an age specific computed cranial focal point.[12] Future conversion of historically manual steps to automated processes will further increase our ability to efficiently deploy AI tools in the clinic.

Pending the future adoption of AI diagnostic tools for plagiocephaly at the community level, research into changing referral patterns and age-at-diagnosis would inform us of the true value of such technologies. As is discussed in Chapter 2, a 1-2 month decrease in the average age

of diagnosis for positional plagiocephaly has the potential to massively decrease costs at the population level. Particularly in the context of the socialized medical system we employ in Canada, the reduction of cost to the healthcare system in one domain allows for the reallocation of resources to another that is sorely pressed for additional support.

Finally, this work serves as a reminder of the pace at which the medical sector has been innovating. The systematic review conducted in Chapter 3 shows us that the integration of AI in diagnostic tools for cranial deformities only began within the last 5 years, with almost all studies since then including a form of automated diagnosis. Recent studies, including ours, have demonstrated diagnostic accuracies well above 80%, suggesting that we have been successful at creating capable diagnostic tools.[8-11] Though these solutions are not without fault, as was discussed earlier, it will be important to critically evaluate past work to continue pushing the envelope to deliver ever more capable systems. In particular, we believe that this work will act as a launchpad for the future development of AI systems that leverage common smartphone platforms for increased availability and ease-of-use.

Chapter 6 – Conclusions

This Thesis aimed to comprehensively evaluate the field of diagnostic modalities for positional plagiocephaly, and to evaluate the clinical performance of a novel AI-based diagnostic solution. A systematic review assessed the available diagnostic modalities and found that though there exists a wide range of capable tools, the majority suffer from equipment requirements or high costs which impede widespread adoption at the primary care level. Further, a practical review explored the financial and intangible costs of a plagiocephaly diagnosis, revealing that a diagnosis given at a later age (i.e. 7 months instead of 4 months) can increase the financial cost of treatment by as nearly 350%. We also discussed the increase emotional burden place on families and caregivers when treatment is prolonged and more involved due to a delayed diagnosis and treatment initiation. Finally, we presented the results of a multi-site clinical validation study which demonstrated that a novel AI based tool, ported to work on a smartphone, could deliver a diagnostic accuracy above 85% while being easy to implement and without requiring expensive or difficult to obtain equipment. Overall, this work demonstrates that there remains a clear need for improved diagnostic tools in the primary care setting, and takes a first step in demonstrating that the solution to this need could very well be found in the marriage of AI and modern day smartphones. Despite this, continued research is needed to further validate the results obtained in this thesis and confirm that AI can safely and suitably be implemented on a broad scale at the community level.

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