Cranial Ultrasound as a First-Line Imaging Examination for Craniosynostosis

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BACKGROUND: Radiography, typically the first-line imaging study for diagnosis of craniosynostosis, exposes infants to ionizing radiation. We aimed to compare the accuracy of cranial ultrasound (CUS) with radiography for the diagnosis or exclusion of craniosynostosis.

METHODS: Children aged 0 to 12 months who were assessed for craniosynostosis during 2011–2013 by using 4-view skull radiography and CUS of the sagittal, coronal, lambdoid, and metopic sutures were included in this prospective study. Institutional review board approval and parental informed consent were obtained. CUS and radiography were interpreted independently and blindly by 2 pediatric radiologists; conflicts were resolved in consensus. Sutures were characterized as closed, normal, or indeterminate. Correlation between CUS and radiography and interreader agreement were examined for each suture.

RESULTS: A total of 126 children (82 boys, 64.5%) ages 8 to 343 days were included. All sutures were normal on CUS and radiography in 115 patients (93.7%); craniosynostosis of 1 suture was detected in 8 (6.3%, 5 sagittal, 2 metopic, 1 coronal). In 3 cases the metopic suture was closed (n = 2) or indeterminate on CUS (n = 1) but normally closed on radiography. CUS sensitivity was 100%, specificity 98% (95% confidence interval 94%–100%). Reader agreement was 100% for sagittal, coronal, and lambdoid sutures (κ = 0.80); after consensus, disagreement remained on 3 metopic sutures.

CONCLUSIONS: In this series, CUS could be safely used as a first-line imaging tool in the investigation of craniosynostosis, reducing the need for radiographs in young children. Additional assessment may be required for accurate assessment of the metopic suture.

WHAT’S KNOWN ON THIS SUBJECT: In many pediatric practices, the first-line imaging modality for evaluation of the cranial sutures is a 4-view cranial radiograph. Cranial ultrasound is an alternative technique for diagnosis or exclusion of craniosynostosis that is radiation-free and technically simple.

WHAT THIS STUDY ADDS: In young children referred for evaluation of the cranial sutures, we found that cranial ultrasound could replace radiography as the first-line imaging study for diagnosis or exclusion of craniosynostosis, reducing exposure to ionizing radiation in this vulnerable population.

Dr Rozovsky conceptualized and designed the study, and drafted the initial manuscript; Drs Udjus and Wilson recruited patients, supervised the cranial ultrasound studies, contributed to data acquisition, and reviewed and revised the manuscript; Mr Barrowman designed the data collection instruments, provided statistical analyses, and critically reviewed the manuscript; Dr Simanovsky contributed to the conception and design of the work, and reviewed and revised the manuscript; Dr Miller contributed to the conception and design of the work, to acquisition, analysis, or interpretation of data, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

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Craniosynostosis, defined as the premature closure of ≥1 cranial sutures, is the most frequent craniofacial anomaly, occurring in 4 to 6 infants per 10,000 live births. Craniosynostosis can present as an isolated finding or in association with various syndromes. Although an isolated single cranial suture closure usually causes only cosmetic deformity, poor gross motor function and learning difficulties resulting from even a single suture synostosis have been reported. Multiple suture synostosis, usually syndromic, has been associated with several complications, such as increased intracranial pressure, headaches, and delayed neurodevelopment.

The initial imaging study for infants with suspicion of this condition is generally 4-view radiography followed by computed tomography (CT) in cases of positive or equivocal findings at radiography. CT with 3-dimensional reconstruction delineates the diagnosis and guides preoperative management.

Cranial ultrasound (CUS) is an alternative imaging modality that is underused in this context. It offers excellent imaging of superficial structures with the potential to confirm or exclude fusion of cranial sutures while avoiding exposure to ionizing radiation in the very young infant. The normal gap of a patent suture (Fig 1) or the obliteration in craniosynostosis can be clearly demonstrated with CUS in children <12 months of age.

Data in previous publications support CUS as an easy and feasible imaging technique for assessment of the cranial sutures. In recent study by Linz et al, CUS confirmed a clinical diagnosis of craniosynostosis or plagiocephaly in a large group of infants.

Most studies have compared CUS with CT and have successfully demonstrated the accuracy of CUS for the detection or exclusion of craniosynostosis. The lack of a larger series comparing findings of CUS with plain radiographs in this setting may be partly responsible for the underutilization of CUS as a first imaging tool for the detection of craniosynostosis.

We aimed to determine whether CUS could replace radiography for the detection of craniosynostosis. The specific objective of this prospective study was to compare the accuracy (sensitivity and specificity) of CUS (index test) versus radiography (reference standard) for the diagnosis or exclusion of craniosynostosis.

METHODS

Institutional review board approval and written informed consent from

FIGURE 1
Sonographic anatomy of a cranial suture. The figure was created based on sonographic-histologic correlation, provided by Soboleski et al. Transverse sonogram of coronal suture demonstrates hypoechoic gap (horizontal arrow) between hyper-echogenic bony plates of the skull (diamond shapes). Asterisk indicates soft tissues of the scalp. Solid arrowhead points to the thin line of dural interface.

FIGURE 2
Flowchart of the study.
parents or guardians were obtained for this prospective study.

**Subjects**

Consecutive patients aged 0 to 12 months who were referred to the Children’s Hospital of Eastern Ontario, Ottawa, Canada, from March 2011 to September 2013 for radiographic evaluation due to a suspicion of craniosynostosis were eligible for inclusion. On presentation to the department, a researcher (E.M., K.R., K.U., N.W.) approached the parent or guardian before radiographs were obtained for consent to perform CUS. Children were excluded if their parent or guardian did not consent or if CUS images were suboptimal due to poor cooperation.

**Imaging Protocols**

The order of imaging was always radiography first and then CUS. Anterior-posterior Caldwell, anterior-posterior Towne, lateral, and submentovertical skull radiographs were obtained as per departmental protocol (kV 77, mAs 1.0–2.0 depending on patient size and density; Digital Diagnostic, Philips HealthCare, Eindhoven, Netherlands).

All 5 departmental sonographers had been previously trained by 2 radiologists (K.R., E.M.) for CUS assessment of the cranial sutures by using the cranial suture simulator model recommended by Ngo et al. A senior radiologist with 5 to 25 years of experience in pediatric ultrasound studies was present during the entire CUS (E.M., K.R., K.U., N.W.). Radiologists, sonographers, and family members were blinded to the findings at radiography during the CUS examination.

CUS was performed by using a 12-MHz linear transducer (IU22 Image System; Philips HealthCare) with the child placed supine or in a semisitting position on a parent’s lap, with the head mildly tilted for

**FIGURE 3**

Assessment of the cranial sutures in a 7-month-old boy, referred to exclude craniosynostosis. A–F: CUS demonstrated normal sagittal, right and left coronal, right and left lambdoid, and metopic sutures (arrows). Note the absence of a hypoechoic gap for the metopic suture. This is the characteristic appearance of a normally closed metopic suture.
optimal sonographic penetration. The CUS study focused solely on evaluation of the sagittal, coronal, lambdoid, and metopic sutures. The transducer was oriented perpendicular to the long axis of the suture being examined, along its entire course. The metopic suture was scanned between the frontal bones, limited posteriorly by the anterior edge of the anterior fontanel. The sagittal suture, which divides the right and left parietal bones, was scanned from the posterior edge of the anterior fontanel to the anterior edge of the posterior fontanel. The left and right coronal and lambdoid sutures were scanned from the midline (lateral edges of the anterior fontanel for coronal sutures and posterior fontanel for lambdoid sutures) to the periphery. Total CUS time was ≤20 minutes. CUS images were recorded and stored in the picture archiving and communication system (PACS) system as a research study with a unique research study number.

**Image Interpretation Protocol**

To standardize the approach, 5 randomly chosen studies (radiographs and CUS) were interpreted in consensus by 2 pediatric radiologists (E.M., K.R., 11 and 7 years of experience, respectively) during data acquisition. Approximately 3 months after closure of data acquisition, the same 2 radiologists independently interpreted all radiography and CUS studies. The readers were blinded to clinical indications and previous reports. During the review, all the CUS studies were interpreted first, before radiography studies, to ensure that the radiographic images would not influence interpretation of CUS. Discrepancies between readers were resolved in consensus.

Findings were documented on the hospital’s Research Electronic Data Capture (REDCap) system (REDCap Consortium, http://www.project-redcap.org/).

**Qualitative Interpretation**

CUS and radiographic examinations were categorized for each suture as normal (hypoechoic gap between the bones, equivalent to patent suture), closed (no hypoechoic gap between the bones, suggestive of bridging or bone deformation), or indeterminate. Because physiologic closure of the metopic suture occurs during the first year, the definition of a “normal” metopic suture included either patent (when a hypoechoic gap was present) or normally closed (absence of a hypoechoic gap with no ridging of the sutures in children >3 months of age). Craniosynostosis was defined as the presence of at least 1 abnormally closed suture.

**Comparison of CUS to CT**

A small number of CT studies that had been performed for study participants were identified and reviewed by the readers only after all CUS and radiographs had been interpreted.

**Statistical Analysis**

With radiography as the reference standard, the sensitivity and specificity of CUS were computed using the Wilson score method. The extent of agreement between readers on qualitative assessment of suture patency on radiographic and CUS studies was evaluated by using the Cohen unweighted $\kappa$. Statistical analyses were performed by using SPSS (IBM SPSS Statistics for Windows, version 22.0; IBM Corp, Armonk, NY) and R version 3.1.0 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria).

**RESULTS**

**Subjects**

Among 150 consecutive patients evaluated by radiography, 21 parents did not consent to the CUS study, either because the parents did not have time to wait for the study or were reluctant to expose the infant to further medical examinations. From the 129 consented children who underwent CUS, 3 patients were excluded because their studies were suboptimal due to poor cooperation...
The study group thus included 126 patients (male-to-female ratio, 82:44; mean age 168.4 ± 2.7 days, range 8–343 days, or 5.5 months, range 0.26–11.27 months) (Fig 2).

Clinical indications for radiography included small or prematurely closed fontanels (51 patients), suspected closed lambdoid sutures/plagiocephaly (right side 14 patients, left side 9, unspecified side 23), suspected closed sagittal suture (7 patients), closed coronal suture (right side 5 patients, left side 5), metopic synostosis (5 patients), and small head circumference (4 patients). In 18 other patients, the indication provided by the clinician was “rule out craniostenosis.” Other indications included macrocephaly (4 patients), and bony ridge anterior forehead, posterior midline bump, septo-optic dysplasia, genetic syndrome not yet diagnosed, or neonatal Graves’ disease (1 case for each indication).

Qualitative Suture Assessment on CUS and Radiography

A total of 115 (91.3%) of 126 patients had normal sutures on both CUS and radiography studies (Figs 3 and 4). A single closed suture was depicted with both imaging modalities in 8 infants (6.3%), including sagittal sutures in 5 children aged 2.1, 2.2, 3.8, 4.3, and 5.5 months (Fig 5); metopic sutures in 2 children aged 2.3 and 5.3 months (Fig 6); and a right coronal suture in 1 child aged 0.5-month (Fig 7). No cases of multiple suture closure were detected on either CUS or radiography.

There was complete agreement between CUS and radiograph for the sagittal, coronal, and lambdoid sutures (κ = 1). In 3 cases there was disagreement between CUS and radiographs regarding the status of the metopic sutures. On CUS examination, the metopic suture was found to be closed (synostosis) in 2 boys aged 8 months old and indeterminate in an 11-month-old girl, whereas it was depicted as normally closed on radiography in all 3 cases (κ for metopic suture = 0.56) (Fig 2). Overall, CUS sensitivity was 100%, specificity was 98% (95% confidence interval 94%–100%).

Interobserver Agreement

Interobserver agreement for the presence of any closed suture by CUS was high (κ 0.80). There was agreement between the readers on 122 (96.8%) of 126 CUS studies. There was disagreement regarding the interpretation of the metopic suture in 4 cases. At consensus interpretation of the CUS studies, these metopic sutures were considered closed normally in 2 cases, closed with synostosis in 1 child (Fig 6), and indeterminate in 1 case. All of these sutures were considered “normally closed” on radiography. CT was not performed in any of the 4 children.
There was disagreement in the interpretation of radiography study for metopic sutures in 5 patients. All cases were resolved in consensus, and the consensus interpretation was then used as the reference standard in these cases. In 3 of 5 cases, there was disagreement in interpretation of CUS as well.

In 1 girl aged 5 months old, the metopic suture was considered closed (synostosis) by 1 reader and “normally closed” by another on radiography; it was called as “closed (synostosis)” in consensus reading. On CUS, the suture was called “closed (synostosis)” by both readers. In an 8-month-old boy, the suture was considered closed (synostosis) by 1 reader and “normally closed” by another on radiography; it was interpreted as “normally closed” after consensus. The suture was called “closed (synostosis)” by both readers on CUS.

**Comparison of CUS to CT**

Cranial CT was performed in 11 (8.7%) of 126 children at the request of the referring physician. CT was performed for surgical planning in cases in which craniosynostosis was diagnosed on radiography (6 children), when there was a suspicion of synostosis and findings at radiography were equivocal (4 children), and in 1 case of accidental trauma. Findings at CT were consistent with radiography and CUS in all 11 cases. In 6 cases of craniosynostosis (true-positive cases), there was closure of the sagittal suture in 4 children (Fig 5), the coronal suture in 1 (Fig 7), and the metopic suture in 1.

In 5 of 11 infants, the sutures were normal. The referring physician requested CT evaluation of the sagittal and lambdoid suture, respectively, in a 1.5-month-old boy and a 9-month-old girl, despite normal cranial radiography. CT was ordered for a 7-month-old boy after right plagiocephaly was seen on radiography; on CT, the sutures were normal (Figs 3 and 4). CT was ordered for a 7-month-old boy with a small fontanel in spite of negative radiography and CUS. This CT study was prompted by the radiologist’s report of cranial radiograph, which contained a comment on sclerotic changes of the metopic suture. The metopic suture was closed normally on CT. Another CT was prompted by an unrelated accidental trauma in a 5-month-old girl who had been examined at age 3 months for suspected premature closure of left coronal and lambdoid sutures. The sutures were normal on radiography and CUS, and remained patent at the time of the CT.

**DISCUSSION**

In the current patient series, CUS performed by sonographers in ≤20 minutes provided good accuracy for the detection of craniosynostosis with 100% sensitivity and 98% specificity (95% confidence interval 94%–100%) in comparison with 4-view radiographs. There was full agreement in interpretation of radiography and CUS for the sagittal, coronal, and lambdoid sutures; there was disagreement between the 2 studies for assessment of the metopic suture in 3 of 126 children.

Previous studies evaluating the accuracy of CUS for evaluation of the cranial sutures have compared CUS with CT.\(^{15,16,18,19,21,23,24}\) Regelsberger et al\(^{16}\) reported 100% success of CUS in the detection of craniosynostosis in 26 patients proven to have this condition on CT. Sze et al\(^{24}\) used CUS...
for evaluation of the lambdoid suture in 41 children undergoing CT scan for suture assessment, and found a mean sensitivity and specificity of 100% and 89%, respectively. Houman Alizadeh et al15 studied 44 children aged <1 year with a diagnosis of synostosis, and demonstrated a sensitivity, specificity, and positive and negative predictive for CUS versus CT scan of 96.9%, 100%, 100%, and 92.3%, respectively. However, to our knowledge, previous studies have not compared the accuracy of CUS and radiography in this setting. Therefore, the purpose of this study was to take a step back before CT is considered and compare findings from cranial radiographs and CUS in the diagnosis of craniosynostosis.

In cases in which craniosynostosis is suspected, an accurate diagnosis is essential. Although craniosynostosis is the most frequent craniofacial anomaly, premature closure of cranial sutures is an uncommon condition.13 Imaging studies rule out abnormal suture closure in most cases. In our study, as expected, the great majority of children (93.7%) had a negative radiograph. However, radiographic studies expose these very young children, who are particularly sensitive, to the deleterious effects of ionizing radiation.26 Reliance on radiography in cases in which there is an alternative imaging technique that avoids exposure to ionizing radiation contradicts the principles of “as low as reasonably achievable” and “image gently” recommendations.27

To date, ultrasound has not shown any harmful biological effects in children and is routinely used for evaluation of the neonatal brain.

The imaging workup in cases of suspected craniosynostosis is affected by referral patterns. In some centers the diagnostic algorithm may vary from clinical evaluation only to the use of different imaging modalities, depending on the preferences of referring physicians. Schweitzer at al28 described their experience with evaluation of children with single lamboid suture craniosynostosis or positional plagiocephaly. In 133 (97%) of 137 infants, the diagnosis was made with clinical examination and no imaging studies were required. In a recent publication by Linz et al,22 the diagnosis of positional plagiocephaly was made by clinical examination alone in 258 of 261 cases, whereas in 3 children, the final diagnosis became possible only after CUS examination. CUS confirmed the clinical diagnosis in 261 of 261 children with positional plagiocephaly and in 8 of 8 cases of lambdoid synostosis. In both of these studies, the clinical diagnosis was made by experienced pediatric neurosurgeons, which should be

FIGURE 7
A 15-day-old girl was referred for cranial suture evaluation due to plagiocephaly. CUS depicted a closed right coronal suture (B, arrow) with bridging of the bone and a patent left coronal suture at the same level (A, arrow). C, Frontal cranial radiograph in the same patient showed right coronal synostosis with a "harlequin eye" on the right side (arrow). D, Three-dimensional reconstruction of cranial CT confirmed abnormal closure of the right coronal suture (arrow).

FIGURE 8
Recommended algorithm for diagnosis or exclusion of nonsyndromic craniosynostosis by pediatrician or family practitioner.
the ideal practice. However, in many places throughout the world, access to a neurosurgeon is low, and responsibility for making the initial diagnosis rests with a family practitioner or pediatrician. In this setting, imaging studies are essential. When imaging is key to the diagnosis, we suggest that CUS may become the first-line technique, avoiding routine use of radiography as an initial examination (Fig 8).

CUS is a short, simple, and inexpensive study, and may be performed by ultrasound specialists with minimal additional training by an experienced ultrasonographer. In comparison with skull radiography, infants are in a more comfortable position during the CUS studies; they can sleep or even be fed during the examination.

In the current study, interpreting radiologists who blindly and independently interpreted both radiography and CUS studies were in full agreement in their assessments of the sagittal, coronal, and lambdoid sutures; however, in 3 cases they disagreed regarding the status of the metopic suture. Metopic synostosis continues to represent a debate in the radiology and neurosurgery communities, and can be difficult to evaluate as children grow because this suture normally tends to close early. In contrast to radiographs, a radiologist performing or supervising the CUS has the opportunity to clinical visualize the forehead, and correlate its appearance on ultrasound with age of the infant.

The metopic suture is known to close more rapidly than the other sutures. Vu et al studied the timing of physiologic closure of normal metopic sutures in a 159 CT studies. They reported the earliest evidence of closure at 3 months of age, and by 9 months the metopic suture was closed in 100% of the children. In a study by Weinzweig et al, metopic suture fusion was complete by 6 to 8 months on CT evaluation. In the current series, the youngest age for physiologic fusion of the metopic suture on CUS examination was 4 months and the oldest patient with a patent metopic suture was 9 months of age.

The limitation of our study is the moderate sample size resulted in a relatively small number of closed sutures, which limits the value of assessments of interreader disagreement, because a single disagreement can lead to a greatly reduced $\kappa$. However, the patient population was accumulated over a period of 2.5 years in a tertiary care children’s hospital and this is the largest series evaluating the performance of CUS for detection of craniosynostosis in children, referred for imaging study by pediatricians and family practitioners.

CONCLUSIONS

The current series suggests that cranial ultrasound, a radiation-free technique, could be used as the first-line imaging tool for exclusion or detection of craniosynostosis in children up to 12 months, reducing the need of initial radiographs in young children. Metopic suture evaluation remains challenging for both CUS and radiography, and additional assessment may be required. These findings warrant assessment and replication in larger prospective studies.

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ABBREVIATIONS

CT: computed tomography
CUS: cranial ultrasound
REDCap: Research Electronic Data Capture

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