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ORIGINAL PAPER

Use of black-bone MRI in the diagnosis of the patients with posterior plagiocephaly

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Abstract
Purpose Ionising radiation exposure is especially harmful to brain development. The purpose of this study was to evaluate whether black-bone (BB) magnetic resonance imaging (MRI), a non-ionising imaging method, offers an alternative to ionising imaging methods such as computed tomography (CT) in the examination of cranial deformities.
Methods From 2012 to 2014, a total of 408 children were referred to the Craniofacial Centre at the Helsinki University Hospital for further examination due to flatness of the posterior skull. Fifteen of these patients required further diagnostic imaging. To avoid ionising radiation, we used an MRI protocol that included sequences for evaluation of both brain anatomy and skull bone and sutures by BB-MRI. A semi-automatic skull segmentation algorithm was developed to facilitate the visualisation. Two patients with scaphocephaly were included in the study to confirm the ability to differentiate synostosis with BB-MRI.
Results We obtained informative 3D images using BB-MRI. Seven patients (7/15, 46.7%) had plagiocephaly on the right side and seven on the left side (7/15, 46.7%). One patient (1/15, 6.7%) had symmetric posterior flatness affecting both sides. Neither structural nor signal-intensity alterations of the brain were detected in visual analysis.
Conclusion BB-MRI provides an alternative to CT when imaging craniofacial deformities. BB-MRI provides not only high-quality 3D-reconstructed imaging of the bony structures and sutures but also information on brain structure in one imaging session. With further development, this method could replace ionising radiation-based methods in analysing deformities of the skull.

Keywords Black-bone MRI · Craniosynostosis · Scaphocephaly · Lambdoid synostosis · Positional plagiocephaly

Introduction

Craniosynostosis occurs when one or more of the sutures between the bones of the cranial vault fuse prematurely [1, 2]. Craniosynostosis can occur as part of a syndrome or as an isolated defect (non-syndromic). As a result, the skull shape becomes deformed and brain growth and development may be impaired. The most common craniosynostosis is sagittal synostosis, which occurs in 45% of non-syndromic cases [3].

Plagiocephaly is used to describe an asymmetry or flatness in the posterior cranial vault of the head. Posterior plagiocephaly can be divided into deformational (positional) plagiocephaly and true lambdoid synostosis [4]. Unilateral lambdoid synostosis occurs only once in every 40,000 live births, accounting for up to 1 to 4% of all patients with craniosynostosis [5]. In contrast to lambdoid synostosis, positional plagiocephaly is a common finding. Depending on the study, current estimates indicate an incidence of 8.2 to 13 to 48% of children under 1 year [6–8]. The incidence of posterior plagiocephaly has increased dramatically over the past two decades since initiation of the “back to sleep” campaign in 1992 by the American Academy of Pediatrics [9]. In clinical practice, it is important to differentiate true lambdoid synostosis from the more common deformational plagiocephaly, which may be

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caused by external forces on the skull or in some cases, a primary growth problem in the brain itself [10, 11]. Posterior plagiocephaly seems to be associated with early neurodevelopmental defects, such as delayed speech development or motor function [12, 13]. Thus, regardless of the cause of posterior plagiocephaly, it is important to screen patients in infancy so that appropriate diagnosis, possible further examinations, and final treatment can be implemented.

The diagnosis of craniosynostosis is made by physical examination and medical imaging. Despite exposure to ionising radiation, the current golden standard for diagnosis is low-dose computed tomography (CT) [14]. The risks associated with radiation exposure are well known [14–17]. Magnetic resonance imaging (MRI) is superior to CT in most cases when evaluating structural brain alterations in children. Thus, in children with craniosynostosis, MRI is routinely performed on patients with neurological symptoms. A non-ionising imaging modality should be the first-choice imaging method in children. However, due to the poor ability of routine MRI sequences to show bony details, MRI thus far has not had a role in diagnostic evaluation of children with skull deformities [18]. In 2012, Eley et al. presented a novel black-bone MRI (BB-MRI) sequence in order to differentiate bone from an almost uniform contrast of soft tissues [19]. The BB-MRI sequence provided improved contrast between soft tissue and bone and enabled 3D rendering of the skull [19–21]. However, the BB method described previously was not as accurate as CT in visualising skull bone and the sutures.

The purpose of this study was to develop and evaluate whether BB-MRI could offer an alternative diagnostic method instead of CT in the examination of skull deformities. We report the imaging protocol, semi-automatic segmentation algorithm, results, and our experience of using BB-MRI as a diagnostic method in children with posterior plagiocephaly.

Patients and methods

Ethical approval for the use of black-bone MRI was granted from the Helsinki University Hospital Research Ethics Committee. From 2012 to 2014, a total of 408 children were referred to the Craniofacial Unit at the Helsinki University Hospital for further examination due to flatness of the posterior skull (i.e. posterior plagiocephaly). Those patients who did not have any neurological symptoms and clearly had positional plagiocephalies were not considered to require further examinations. In this study, MRI of the skull and brain was performed when the patient had a severe posterior plagiocephaly that did not show any improvement before the age of 18 months and was accompanied with neurological symptoms. Thus, MRI was used for diagnostic evaluation of patients with severe posterior plagiocephaly and neurological concerns, including motor skill delays (3/15 patients, 20%), delayed speech development (11/15 patients, 73.3%), dysphasia (1/15 patients, 6.7%), or behavioural problems (5/15 patients, 33.3%).

The accuracy and diagnostic value of BB-MRI to exclude synostosis were tested in two patients with scaphocephaly. For these patients, the indication for MRI was the preoperative evaluation of potential intracranial findings (such as Chiari malformation). BB-MRI imaging was performed in the same imaging session.

All imaging was performed under generalised anaesthesia. Images were acquired with a 3-T Siemens Verio or Skyra (Erlangen, Germany) and a 32-channel head coil. The imaging protocol included anatomical sequences (i.e. axial T2-TSE, T13D, and a 2D FLAIR for radiological evaluation) and a BB-MRI sequence. The BB-MRI sequence was based on the work by Eley et al. [19, 21–25]. We also used MRI-based radiation therapy planning and attenuation correction for PET-MRI, where in-phase and out-of-phase imaging (i.e. Dixon technique) [26] is used for the generation of the so-called pseudo-CT [27, 28]. The sequence evolved during the study and the currently used BB-MRI sequence at our hospital is an axial or sagittal (or both) T1 VIBE sequence, where both in-phase and out-of-phase images are acquired at a resolution of $1 \times 1 \times 0.9$ mm^3, interpolated in-plane resolution of 0.5×0.5 mm^2, FOV 192 $*$ 192, TR 25 ms, flip angle 3° or 5°, and NSA 1, with distortion correction applied. The acquisition time is about 2.5 min, depending on the number of the slices required for full head coverage.

The skull is segmented from the BB-MRI images semi-automatically with a Matlab (MathWorks Inc., USA) script. First the in-phase and out-of-phase images are separated and reoriented with FMRIB FSL tools [29, 30] and zero-padded by 10 voxels. The in-phase image was segmented into background and foreground by applying Otsu thresholding [31] to each slice separately, and to obtain an intact foreground, mask dilation/erosion image operations were performed. A rough initial skull segmentation can already be obtained from the Otsu thresholding. The fat image was calculated from the in-phase and out-of-phase images [26] and segmented into two categories (background mean of the fat image, 0.5 $*$ maximum value of the fat image) with the 3D bias field-corrected fuzzy c-means clustering (BCFCM) algorithm [32] as implemented previously (https://se.mathworks.com/matlabcentral/fileexchange/25712-bias-field-corrected-fuzzy-c-means). The fat mask was obtained from the probability map by thresholding with a value of 0.7. Excluded areas from the foreground mask were categorised as fat, which is a simple way to avoid false categorisation (e.g. due to a chemical shift artefact in the in-phase image). The masked in-phase image was also segmented with the 3D BCFCM-algorithm initiated with five intensity values (background mean, 0.5 $*$ mean of the Otsu-thresholded skull, mean of the Otsu-thresholded skull, 0.5 $*$ image maximum value, 0.75 $*$ image maximum value). This resulted in five different probability images; of which, only the two probability images initiated with the Otsu-thresholded skull intensities were summed. For the summed probability map, a threshold value of approximately 0.3 was used and a skull mask was obtained. The inverted in-phase image was then masked with this skull mask.

The image visualisation was performed with 3D Slicer [33]. The segmentation was visually assessed and manually improved if necessary. If the segmentation required manual improvement, typically bias field correction was performed on the original in-phase image using the N4ITK bias field correction module [34]. All MR images were analysed by a neuroradiologist (NB) who had 11 years of experience in radiology.

Results

We obtained informative 3D images of the skull bone and posterior sutures by using BB-MRI in 15 patients with posterior plagiocephaly (Figs. 1 and 2). The mean age at time of imaging was 38.4 months (SD 12–84 months). Seven patients (7/15, 46.7%) had right posterior plagiocephaly and seven (7/15, 46.7%) patients had left-sided posterior plagiocephaly. One patient (1/15, 6.7%) had symmetric posterior plagiocephaly affecting both sides.

The patients with posterior plagiocephaly had neither structural nor signal-intensity alterations of the brain. Cranial sutures of all patients with posterior plagiocephaly were open, and no patients had lambdoid synostosis (Figs. 1 and 2). For the first 10 patients with positional plagiocephaly, we confirmed the suture diagnosis with CT in addition to MRI. However, for most of the patients, the diagnostic quality of the BB-MRI images alone was sufficient.

To further confirm the diagnostic value of BB-MRI in visualising synostotic sutures, two patients with scaphocephaly were imaged by MRI using black-bone sequences (Fig. 3a–b). The BB-MRI for these two patients was performed with 3D gradient echo FLASH sequences; the image quality required improvement. Sequence type was changed to a VIBE (Fig. 1). Slight adjustment to the sequence was later performed (e.g. increasing the resolution and also aquiring the out-phase image). A segmentation algorithm was developed and utilised to facilitate better 3D visualisation of the BB-MRIs (Figs. 2 and 3).

The 3D BB-MRI images were considered accurate and showed the structures of the skull adequately (Fig. 2), including the sutures important for diagnosis of sagittal synostosis (Fig. 3). Sagittal sutures of two patients were visualised very similarly in BB-MRI and routine CT 3D reconstruction images. The MRI protocol used provided us with information not only about the skull and sutures but also on the brain structures. Minor left cerebellar hemisphere haemorrhage was identified by the presence of hypointensity on the T2-weighted sequence in one patient with scaphocephaly (Fig. 3b). The same patient also had mild ectopia of the cerebellar tonsils through the foramen magnum.

Discussion

The aim of this study was to assess the use of BB-MRI in the evaluation of skull deformities. The BB-MRI method presented by Eley et al. was used and further developed as a suitable

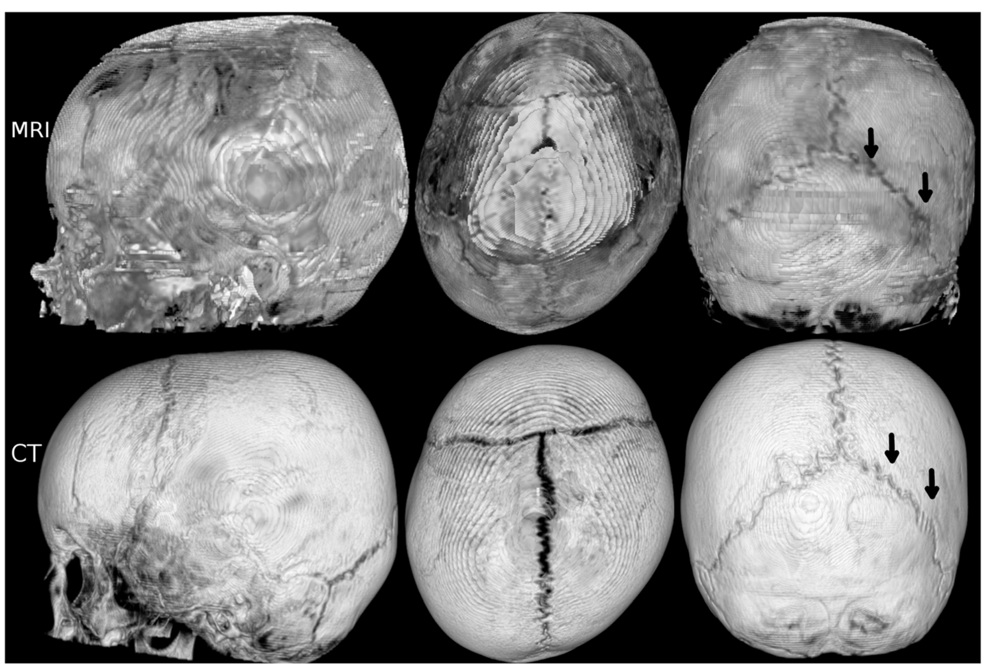

Fig. 1 Skull images of a 32 month (2 year 8 months)-old patient with right posterior asymmetry of the skull. Top row, 3D-rendered BB-MRIs before protocol optimisation. Bottom row, 3D- rendered CT images of the same patient

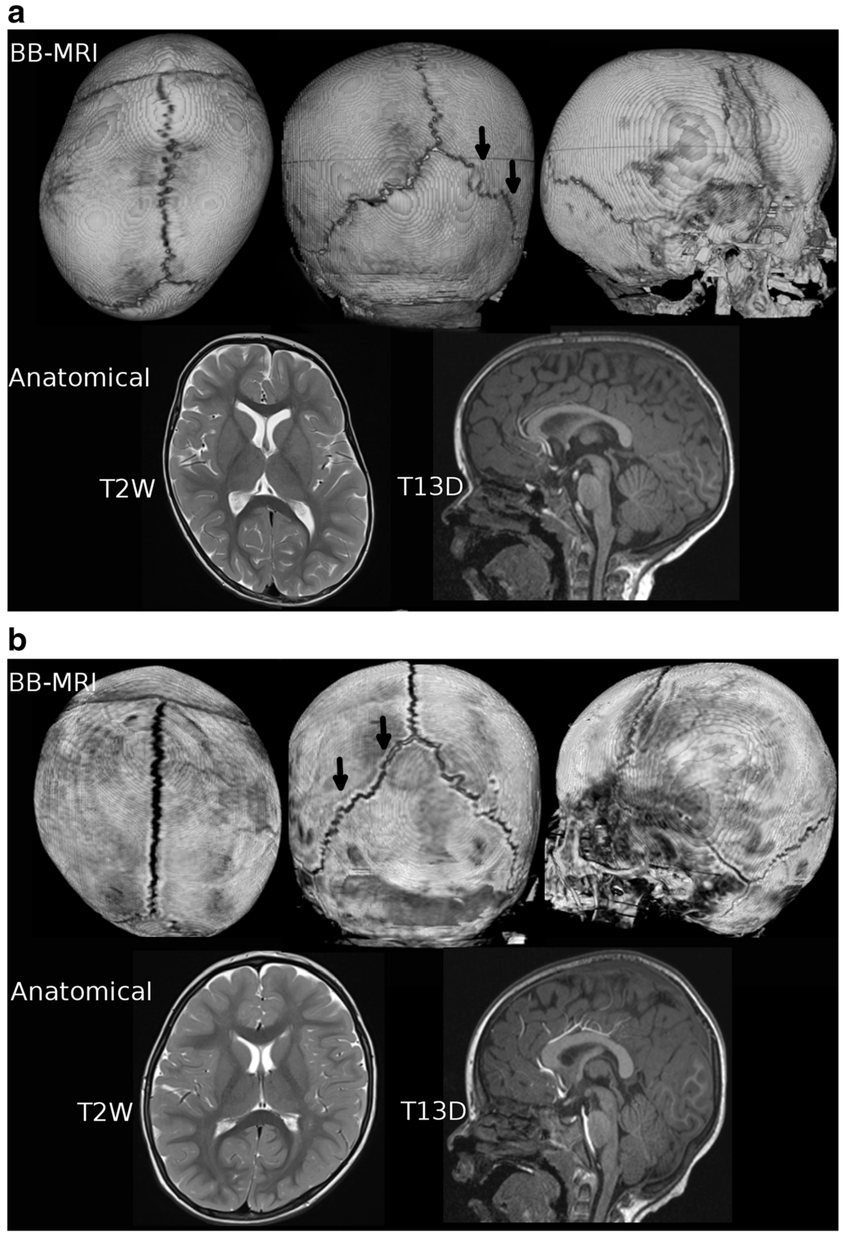

Fig. 2 3D-rendered BB-MRIs and anatomical T2 and T13D images of two patients with posterior plagiocephaly. **a** A 24-month-old (2 years) patient with posterior plagiocephaly. **b** A 25-month-old (2 years 1 month) patient with posterior plagiocephaly. Black arrows on the BB images point to the lambdoid suture on the flat posterior hemisphere. No structural abnormalities were observed in either patient in the anatomical regions

MRI protocol for diagnostic imaging as an alternative for CT. We report our imaging protocol and semi-automatic segmentation method, results, and our experience of using BB-MRI.

In routine diagnostic evaluation of children with deformities of the skull, CT provides the ability to document the patency or closure of the sutures and aid in surgical planning [35]. However, the potential risks associated with radiation exposure are well known [14–17, 36]. In 2012, the American National Cancer Institute raised concerns about the hazards of ionising radiation with regard to inducing tumours and developmental delays in children [36]. Some authors have suggested that CT examination is not justified in craniosynostosis [37, 38]. MRI is a potential tool for imaging patients with cranial malformations and brain structure without harmful radiation [39, 40] and may also possess certain advantages over CT [41].

In most cases, the differential diagnosis of lambdoid synostosis and non-synostotic posterior plagiocephaly is clear only by clinical examination [11]. However, a minority of patients with deformational plagiocephaly present with a severe flatness and require differential diagnostics and imaging [42]. In the case of posterior plagiocephaly, physicians may need information not only on the bony structures of the skull but also on the brain. The cause of unilateral posterior plagiocephaly can be in some cases induced by a primary problem in growth of the brain itself. For these reasons, we included conventional MRI sequences in addition to the BB-MRI sequence to our imaging protocol. To confirm that we

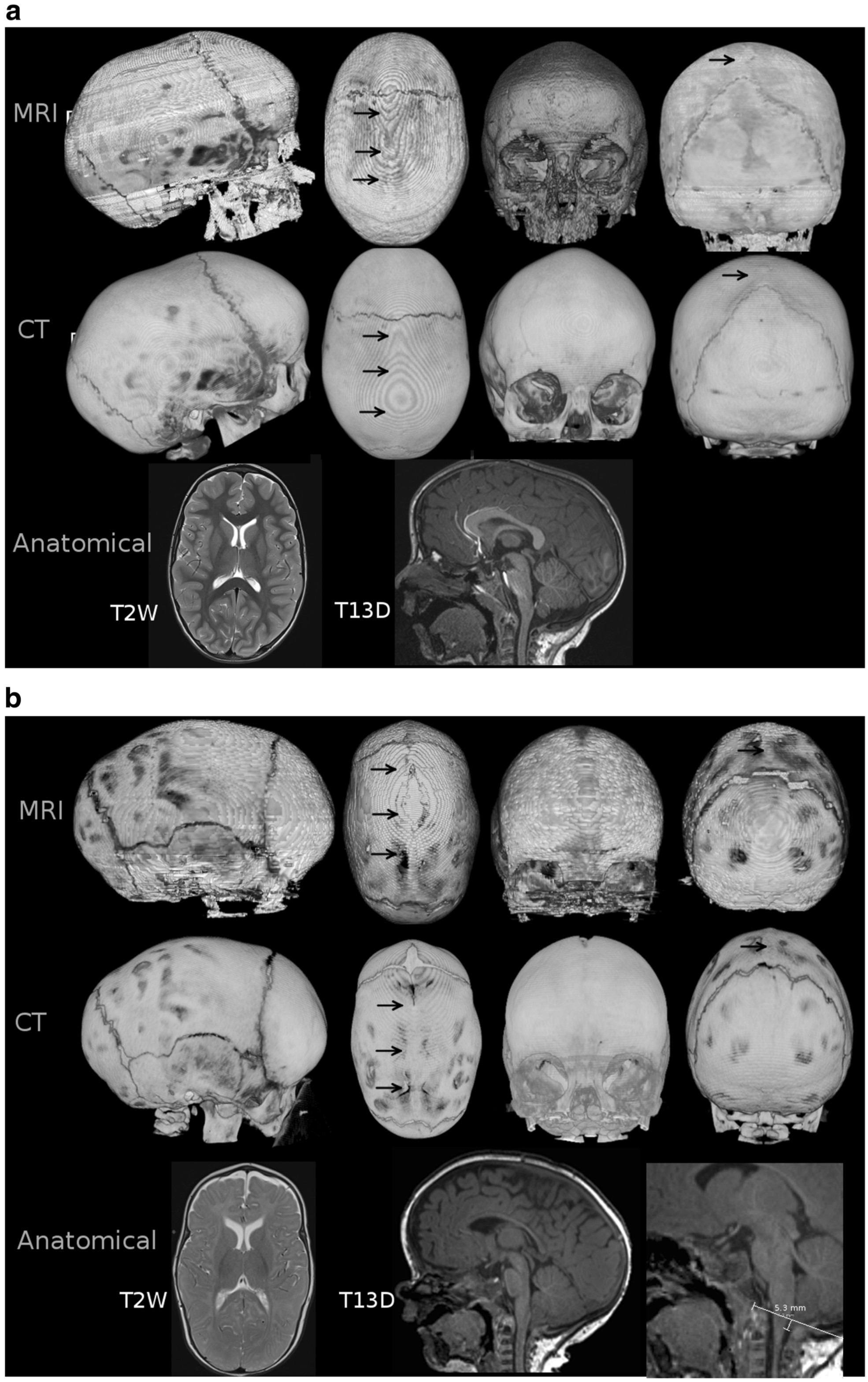

Fig. 3 **a** A 57-month-old (4 years 9 months) patient with sagittal synostosis. Top row, 3D-rendered BB MRIs. Middle row, 3D-rendered CT images. This patient had no structural abnormalities on the anatomical T2W and T13D images, as seen on the bottom row. **b** A 6-month-old patient with sagittal synostosis. Top row, 3D-rendered BB-MRI images. Middle row, 3D-rendered CT images. Bottom row, anatomical T2W and T13D images. Minor left cerebellar hemisphere haemorrhage was observed in the T2 images (not shown), otherwise no abnormal T2 signal changes were detected. Mild ectopia of the cerebellar tonsils through the foramen magnum was observed in the T1 images

can identify synostosis with BB-MRI, two patients with scaphocephaly were evaluated by BB-MRI and routine CT imaging. By both methods, the patient sutures were identified as areas of decreased signal intensity, with these features being absent at the site of synostosis in the sagittal suture.

One major advantage of BB-MRI over CT is the avoidance of harmful radiation exposure. Another advantage of BB-MRI is that information on both the skull and brain can be obtained in one imaging session. In particular, posterior cranial synostoses may be associated with Chiari malformation with herniation of one or both cerebellar tonsils [43]. Of our 15 patients with posterior plagiocephaly, none of the children had structural abnormalities of the brain tissue despite presence of neurological symptoms.

While MRI eliminates the risks of ionising radiation, increased examination time and cost may be disadvantages of this method. However, the black-bone sequence itself lasts approximately 3 min. If there is need to image the brain as well, the whole protocol for clinical purposes is possible to perform in 15 to 20 min. In infants, the longer anaesthesia or sedation time can be considered as a potential risk [44]. However, in children under the age of 6 months, the MRI is possible to perform in natural sleep after feeding. Imaging unanaesthetised children with a less motion-sensitive sequence may be beneficial. The ultra-short TE sequences will also offer new opportunities for craniosynostosis imaging, but the availability of the sequence on current scanners is limited. These imaging sequences may, however, increase the acquisition time.

Eley et al. demonstrated that 3D-rendered images of the skull can be obtained with image processing software [21]. A segmentation algorithm of the skull was used to improve the visualisation, but the algorithm should be developed further. Currently, the segmentation algorithm misclassifies some intracranial structures and manual improvement is required. We have observed that the segmentation of the skull is more difficult the younger the patient is. For example, the skull of a 6-month-old infant is quite thin and has a higher water content, thus the bone is not always black. Therefore, we have decided to postpone preoperative imaging close to the planned surgical session. Also an optimised sequence for infants would be desirable. More studies are needed to decide the optimal age of the infant as far as the interpretation of the imaging is concerned. Our final goal for the segmentation is a fully automatic workflow. This will require registration to a standard space, so that desired projections of the skull can be generated consistently.

In conclusion, the MRI protocol with the BB-MRI sequence used in this study provides a very promising alternative to CT when imaging patients with any calvarial deformity, plagiocephaly, or craniosynostosis. This protocol provides high-quality 3D-reconstructed skull images and visualisation of structural abnormalities of brain structure during one imaging session. We believe that with further development, the method could gain wide acceptance as a method of choice in everyday practice for patients with deformities of the skull. It should also be remembered that although the brain in visual analysis may be considered normal in conventional MRI, the patient can present neurological symptoms. In the future, additional microstructural and functional MRI imaging, such as diffusion tensor imaging (DTI) and resting state functional MRI, could provide more information about the potential underlying microstructural changes in these patients.

Author contribution Kuusela Linda: writing, development of imaging protocol, and analysis of patient material.

Hukki Ada: writing, collecting patient material, and analysis of patient material.

Brandstack Nina: radiologist, analysis of patient material, and writing.

Autti Taina: study design and writing.

Leikola Junnu: collecting patient material and writing.

Saarikko Anne: study design, collecting patient material, and writing.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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