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Diagnosis of Impaired Brain Perfusion in Children with Craniosynostosis by Magnetic Resonance Imaging

Maxim V. Lukin, Yana A. Filin, Daniil A. Beregovskii, Elena D. Vyshedkevich, Alexsander Yu. Efimtsev, Gennady E. Trufanov

Almazov National Medical Research Centre, Saint Petersburg, Russia

ABSTRACT

BACKGROUND: Craniosynostosis is a medical condition characterized by the premature fusion or absence of cranial sutures, leading to an abnormal head shape and a potential risk of neurological disorders. There is a growing interest in the early diagnosis of craniosynostosis. Delayed treatment of synostoses can impede normal cranial bone growth, resulting in cranial deformities, craniocerebral disproportion, and microcephaly. The abnormal head shape may result in the compression of brain tissue, meninges, and vascular structures in the affected regions. Noninvasive imaging techniques are currently available for assessing cerebral hemodynamics. Dynamic susceptibility contrast magnetic resonance perfusion facilitates the evaluation of relative cerebral blood flow in regions suspected of brain compression in pediatric patients with craniosynostoses.

AIM: To evaluate cerebral blood flow in children with craniosynostoses using dynamic susceptibility contrast magnetic resonance perfusion to determine relative hemodynamic parameters, such as cerebral blood flow and cerebral blood volume.

METHODS: The study included a total of 52 children diagnosed with different types of craniosynostosis. The age of the participants ranged from 3 to 38 months. They were assessed using a 1.5T magnetic resonance imaging scanner with an intravenous paramagnetic contrast agent (0.1 mmol/kg of body weight) administered during drug-induced sleep. The standard brain examination protocol was augmented with dynamic susceptibility contrast magnetic resonance perfusion pulse sequences.

RESULTS: A comprehensive analysis of the findings demonstrated that metopic, mono- and bicoronal synostosis were associated with reduced cerebral blood flow and blood volume in the compressed region when compared with the contralateral intact region. In contrast, no significant differences in magnetic resonance perfusion findings were identified between the affected and intact regions for the patients with sagittal craniosynostosis.

CONCLUSION: This study found that dynamic susceptibility contrast magnetic resonance perfusion can be a useful tool for assessing changes in cerebral perfusion. This finding offers novel prospects for planning treatment strategies. The proposed approach has the potential to serve as a valuable tool for patient assessments during both the early and late postoperative periods.

Keywords: dynamic susceptibility contrast MR perfusion; DSC perfusion; craniosynostosis; craniocerebral disproportion; magnetic resonance imaging.

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Диагностика перфузионных нарушений головного мозга у детей с краниосиностозами методом магнитно-резонансной томографии

М.В. Лукин, Я.А. Филин, Д.А. Береговский, Е.Д. Вышедкевич, А.Ю. Ефимцев, Г.Е. Труфанов

Национальный медицинский исследовательский центр им. В.А. Алмазова, Санкт-Петербург, Россия

АННОТАЦИЯ

Актуальность. Краниосиностоз — это состояние, характеризующееся отсутствием или ранним закрытием швов черепа, приводящее к его характерным деформациям и вероятным развитием неврологических нарушений. На сегодняшний день интерес к ранней диагностике краниосиностозов неуклонно растет. Отсутствие своевременной коррекции синостозов приводит к замедлению роста костей черепа, его деформации, краниоцеребральной диспропорции и микроцефалии. Аномальная форма черепа приводит к компрессии вещества головного мозга, его оболочек и сосудов в наиболее деформированных участках. На современном этапе существует ряд методик, позволяющих неинвазивно оценить показатели мозгового кровотока. Динамическая контрастная МР-перфузия позволяет оценить относительные показатели мозгового кровотока в предполагаемых зонах компрессии головного мозга у детей с краниосиностозами.

Цель — провести оценку мозгового кровотока у детей с краниосиностозами с помощью контрастной динамической магнитно-резонансной перфузии, определяя относительные показатели (скорость мозгового кровотока (rCBF,) объем мозгового кровотока (rCBV)).

Материалы и методы. Обследовано 52 ребенка с различными типами краниосиностоза. Возраст участников варьировался от 3 до 38 мес. Исследование проводили с помощью аппарата с индукцией магнитного поля 1,5 Тл, с внутривенным введением парамагнитного контрастного средства в дозе 0,1 ммоль/кг, при этом пациенты находились под медикаментозным сном. Стандартный протокол исследования головного мозга был дополнен импульсной последовательностью динамической контрастной МР-перфузии.

Результаты. Анализ результатов показал, что при метопическом, моно- и бикоронарном синостозах показатели скорости мозгового кровотока и объема мозгового кровотока в области компрессии были ниже, чем в интактной области противоположного полушария. В отличие от этого, при сагиттальном краниосиностозе значимых различий в данных МР-перфузии не выявлено.

Заключение. В нашем исследовании продемонстрировано, что динамическая контрастная МР-перфузия может служить для оценки изменений церебральной перфузии. Это открывает новые возможности для планирования стратегии лечения пациентов. Описанная методика также может стать полезным инструментом для анализа динамики как раннего, так и позднего послеоперационного периода.

Ключевые слова: динамическая контрастная МР-перфузия; DSC-перфузия; краниосиностоз; краниоцеребральная диспропорция; магнитно-резонансная томография.

Как цитировать

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BACKGROUND

Craniosynostosis, also called cranial synostosis, craniostenosis, or simply synostosis, is a congenital condition characterized by the premature closure of one or more cranial sutures. This condition results in characteristic skull deformities, facial asymmetry, and impaired brain development [1]. "Single" synostosis, which involves the premature fusion of a single cranial suture, or "complex" synostosis, which involves more than one suture, may occur as a primary condition (isolated or syndromic) or secondary due to various underlying causes, including metabolic, intracranial, teratogenic, and hematologic conditions [2, 3]. Craniosynostosis may be asymptomatic; however, it often leads to increased intracranial pressure and persistent neurological, auditory, ophthalmologic, and cognitive impairments [1].

Scientific data show that the incidence of craniosynostosis is approximately 1 in 2100–2900 live births, with a higher prevalence in boys than in girls (4:1). It is often present at birth and becomes more apparent during the first few months of life because of visible skull deformities [2]. The most common form is sagittal synostosis, which accounts for 40%–60% of cases, followed by coronal synostosis [3]. In the past two decades, the diagnosis of craniosynostosis has markedly increased compared to previous years.

The increasing interest in craniosynostosis is driven by the increasing incidence of the condition and advances in the understanding of its genetic origins [3]. Etiologically, craniosynostosis is classified as primary or secondary. Primary craniosynostosis is caused by abnormal development during the embryonic period, resulting in premature suture closure. In contrast, secondary craniosynostosis results from mechanical, metabolic, or teratogenic factors affecting the fetus in utero. Approximately 85% of primary craniosynostosis cases are isolated, and 15% are associated with multisystem syndromes. In most cases of isolated craniosynostosis, only one suture is fused. Premature suture closure hinders normal skull growth in the direction perpendicular to the fused suture, and the remaining sutures undergo compensatory growth [4, 5]. Moreover, craniosynostosis can be classified according to skull deformity: scaphocephaly (sagittal suture fusion), trigonocephaly (metopic suture fusion), anterior plagiocephaly (unilateral coronal suture fusion), brachycephaly (bilateral coronal suture fusion), posterior plagiocephaly (unilateral lambdoid suture fusion), turricephaly (bilateral lambdoid suture fusion), oxycephaly (fusion of sagittal and coronal sutures), and cloverleaf skull deformity (fusion of sagittal, coronal, and lambdoid sutures).

Although craniosynostosis can often be diagnosed clinically, determining the full extent of cranial involvement based on physical examination alone can be challenging. The diagnosis is typically confirmed using radiological imaging, particularly in cases of complex synostosis when surgery is being considered [6]. Imaging is crucial for accurate diagnosis, surgical planning, postoperative evaluation, and detection of associated anomalies or complications [7].

Currently, various radiological techniques are employed to diagnose craniosynostosis and associated intracranial conditions; computed tomography (CT) and magnetic resonance imaging (MRI) are the most commonly used modalities [8].

Multislice computed tomography (MSCT) is widely used alongside skull radiography, ultrasound, and MRI for diagnosing and monitoring patients with craniosynostosis [9]. The sutures of the cranial vault and base are most accurately visualized on axial and 3D surface-shaded reconstructions, which are currently the gold standard in the radiologic assessment of craniosynostosis [10]. Preoperative CT imaging is employed to confirm the clinical diagnosis, evaluate structural abnormalities and neurovascular anatomy, and assist in precise surgical planning [11]. Postoperative CT scans can be helpful in identifying potential complications, evaluating surgical outcomes, and assessing the adequacy of calvarial expansion [11].

The advent of MRI has enabled new opportunities for studying brain pathological conditions, including in pediatric practice [12]. Recent technological advancements have enabled more detailed assessment of the brain and its meninges without radiation exposure, which is a major advantage of MRI. However, MRI is less widely used than CT because of limited visualization of bony structures, high cost, long scan duration, and the need for sedation.

Surgical intervention for craniosynostosis is often indicated owing to increased intracranial pressure, hydrocephalus, and craniocerebral disproportion, which are typically associated with syndromic or multisuture nonsyndromic craniosynostosis [13]. Contemporary understanding of the condition indicates that in craniosynostosis, cerebral blood flow disturbances occur primarily due to bony compression at the sites of fused sutures. Moreover, clinical manifestations such as delayed speech development, intracranial hypertension, and auditory and ophthalmological disorders may present at a significantly later stage [14].

In the scientific community, investigations are being conducted to evaluate cerebral perfusion in children with craniosynostosis using single-photon emission CT (SPECT) and MRI employing non-contrast arterial spin labeling (ASL) perfusion methods [15, 16]. However, both techniques have limitations; SPECT involves radiation exposure, and non-contrast MR perfusion does not allow for comprehensive assessment of all cerebral blood flow parameters.

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MR perfusion is widely used in diagnosing malignant brain tumors and acute cerebrovascular events, enabling differentiation between irreversibly damaged areas and those with potentially reversible changes [17]. However, this method remains to be adopted in routine clinical practice for the diagnosis of perfusion abnormalities in children with craniosynostosis. International scientific data show that only a limited number of studies have explored non-contrast ASL perfusion, which yields information solely on cerebral blood flow (CBF) despite not requiring contrast administration [14, 15]. Conversely, dynamic susceptibility contrast (DSC) MR perfusion allows for the evaluation of additional cerebral hemodynamic parameters beyond CBF, including cerebral blood volume (CBV), time to peak (TTP), and mean transit time (MTT).

Measuring tissue perfusion depends on the ability to sequentially determine the tracer agent concentration within the target organ. Previously, exogenous tracers such as chilled saline, iodinated radiographic contrast agents, and radionuclides were used [14]. In recent years, with the advent of MRI, exogenous tracers such as paramagnetic contrast agents and endogenous tracers such as magnetically labeled blood have been used [14].

MR perfusion methods using exogenous tracers are based on a model wherein the tracer is restricted to the intravascular compartment and does not diffuse into the extracellular space. Imaging can be performed dynamically (rapid acquisition during bolus injection) or in a steady state (after achieving equilibrium concentration in blood through continuous infusion). Dynamic imaging takes advantage of transient alterations in the local magnetic field of surrounding tissue caused by the passage of a bolus of paramagnetic tracer through the organ's capillary network. These local magnetic field changes may appear as signal changes on MR images. Time–concentration curves for the tracer can be analyzed to derive various tissue hemodynamic parameters (CBF, CBV, MTT, and TTP). CBF is defined as the volume of blood passing through a given volume of brain tissue per unit time, which is typically expressed in milliliters per minute per 100 g of brain tissue. CBV refers to the volume of blood within a given volume of brain tissue, usually reported as milliliters per 100 g of brain tissue. MTT is calculated by dividing CBV by CBF. TTP is the time it takes for the concentration of the contrast agent to reach its maximum. CBF is obtained using the formula CBF = CBV/MTT [14]. Thus, DSC MR perfusion enables the assessment of relative cerebral perfusion indices in regions suspected of brain compression in children with craniosynostosis.

This study aimed to evaluate CBF in children with craniosynostosis using DSC MR perfusion by determining relative perfusion parameters, namely, relative CBF (rCBF) and relative CBV (rCBV).

METHODS

Fifty-two children diagnosed with various types of craniosynostosis were examined: 12 children (23%) had sagittal suture synostosis, 16 (31%) had metopic suture synostosis, 10 (19%) had unilateral coronal synostosis, 6 (13%) had bicoronal synostosis, 2 (4%) had lambdoid suture synostosis, and 6 (13%) had multisutural craniosynostosis. The age of the participants ranged from 3 to 38 months. All examinations were performed using a 1.5 Tesla MRI scanner (Magnetom Espree, Siemens) under pharmacological sedation, with intravenous administration of a paramagnetic contrast agent at 0.1 mmol/kg.

The standard brain imaging protocol was supplemented with a DSC MR perfusion sequence—"ep2d_perf" (Table 1).

Color-coded perfusion maps of CBF and CBV were generated using the syngo.via software platform (Siemens). Then, regions of interest (ROIs) corresponding to the most compressed cortico-subcortical areas were manually delineated. Subsequently, a mirrored ROI was placed on the contralateral ("unaffected") side for comparison of MR signal intensity. The perfusion index within the compressed area was calculated relative to the intact region as 100% (Fig. 1).

Statistical analysis was performed using the R programming language (version 4.4.1). The mean values of relative perfusion parameters and standard deviations were obtained for each group.

RESULTS

In metopic craniosynostosis (trigonocephaly), the relative values of rCBV and rCBF in the region of compression (frontal lobes) were 87.4% ± 25.5% and 84.6% ± 19.8%, respectively, compared to the parieto-occipital regions (Fig. 1).

In unicoronal synostosis (anterior plagiocephaly), the values in the compression zone (ipsilateral frontal lobe) were 94.5% ± 4.2% (rCBV) and 94.2% ± 3.4% (rCBF) relative to the contralateral frontal lobe and 85.3% ± 4.8% (rCBV) and 88.1% ± 9.1% (rCBF) compared to the occipital lobes (Fig. 2).

In bicoronal synostosis (brachycephaly), the values in the frontal lobes were 85.1% ± 18.9% (rCBV) and 87.3% ± 15.3% (rCBF) relative to the parieto-occipital regions (Fig. 3).

In sagittal suture fusion (scaphocephaly), the relative values in the parietal lobes compared to the frontal and occipital lobes were 98.9% ± 2.2% (rCBV) and 99.5% ± 3.2% (rCBF) (Fig. 4).

Analysis showed that in metopic, unicoronal, and bicoronal synostosis, rCBV and rCBF values were lower in the area of compression than in the intact region of the

Table 1. Pulse sequences and scanning parameters

Sequences	TE, ms	TR, ms	FoV, mm	Slice thickness, mm	Flip angle, degrees
Axial T2-WI	113	4000	230	4	140
Axial TIRM-WI	93	7000	230	4	140
Coronal T2-WI	113	4000	230	4	140
Sagittal T1-MPRAGE (pre- and post-contrast)	2.83	2300	256	1	160
ep2d_perf	1440	51	230	5	90

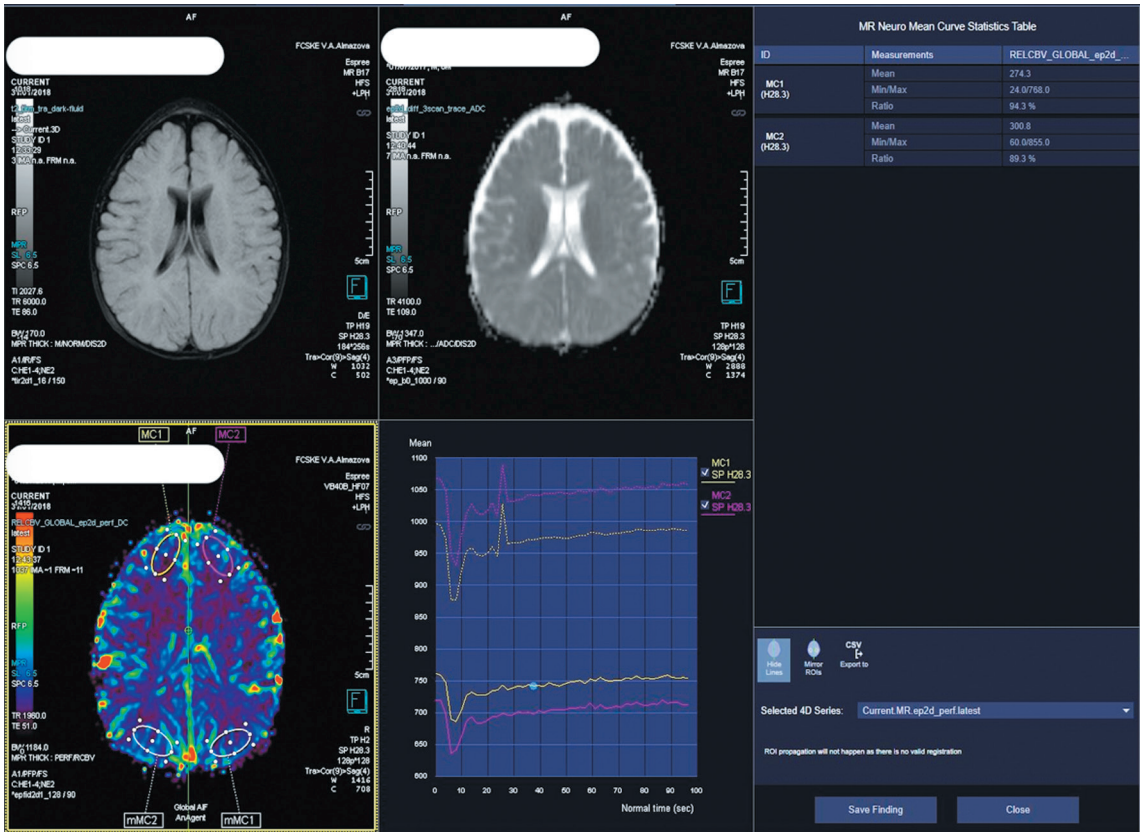

Fig. 1. CBV perfusion map in a patient with metopic synostosis. Arrows: relative perfusion values.

opposite hemisphere. In contrast, in sagittal craniosynostosis, no significant differences were detected in MR perfusion data.

DISCUSSION

Despite the high level of diagnostic methods available, the detection rate of craniosynostosis remains low, particularly at the outpatient stage [13]. The proportion of "neglected" craniosynostosis cases diagnosed in older children is high. Premature fusion of cranial sutures leads to restricted skull growth; however, the brain continues to grow normally, resulting in craniocerebral disproportion. The later craniosynostosis is diagnosed, the more pronounced the disproportion becomes, potentially leading to one of the most serious consequences, namely, intracranial hypertension [18]. Owing to its high resolution and tissue contrast, MRI allows excellent visualization of brain structures and cerebrospinal fluid spaces, enabling the identification of signs of increased intracranial pressure [16]. Additionally, a standard brain MRI protocol supplemented by dynamic contrast-enhanced perfusion imaging provides assessment of cerebral perfusion parameters, serving as an additional criterion for early surgical decision-making. According to some studies, the optimal age for surgical treatment is between 3 and 10 months [8]. Early diagnosis of craniosynostosis during the neonatal period and the first months of life can significantly improve cosmetic and functional treatment outcomes.

Fig. 2. CBF perfusion map in a patient with right-sided coronal synostosis.

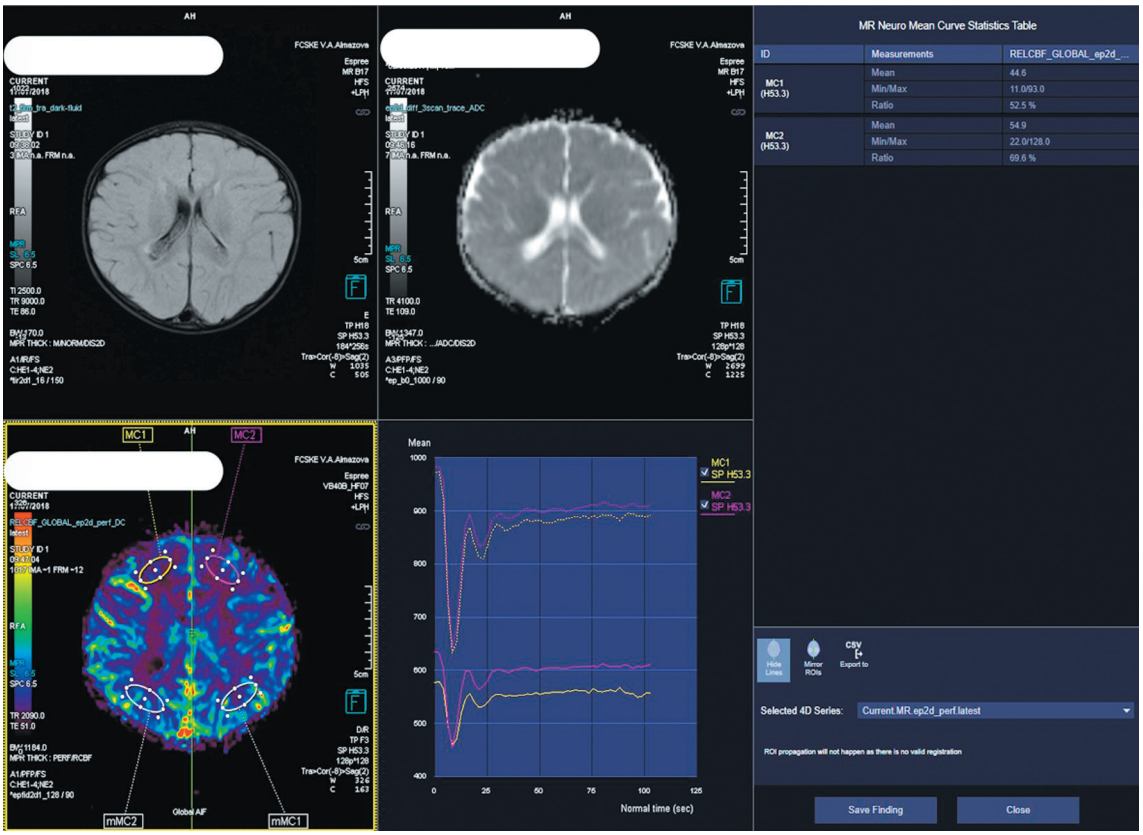

Fig. 3. CBF perfusion map in a patient with bicoronal synostosis.

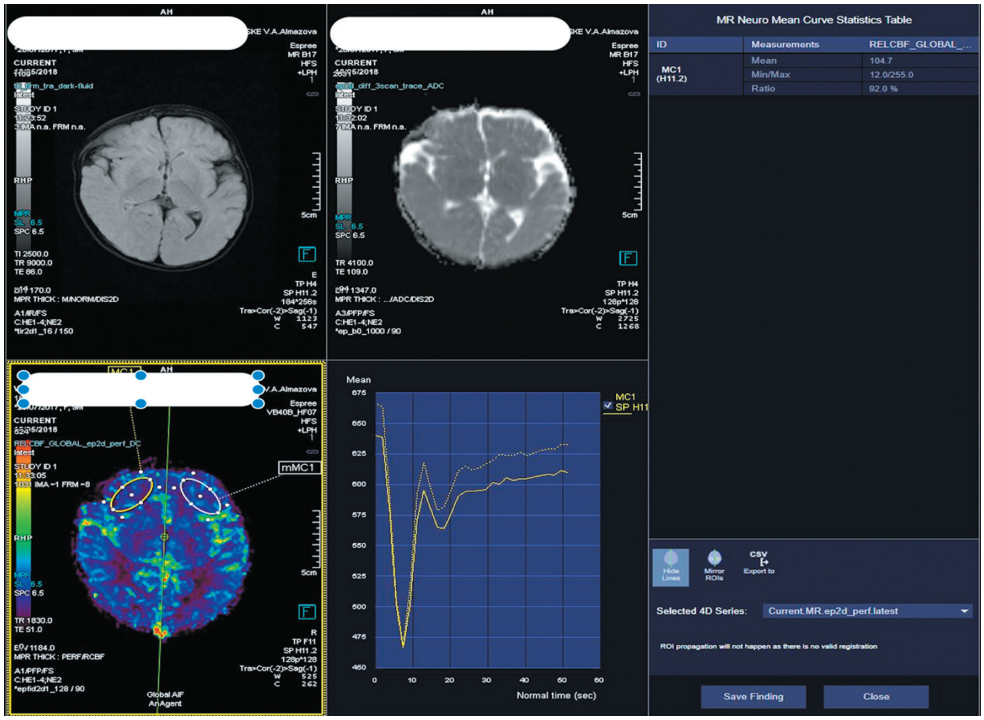

Fig. 4. CBF perfusion map in a patient with sagittal synostosis.

CONCLUSION

This study demonstrates that dynamic contrast-enhanced MR perfusion can be used to assess changes in cerebral perfusion. This opens up new possibilities for planning treatment strategies in patients. Moreover, the described technique may be a valuable tool for analyzing the trends of both the early and late postoperative periods.

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Consent for publication: Written consent was obtained from the patients for publication of relevant medical information within the manuscript.

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AUTHORS' INFO

Maxim V. Lukin, postgraduate student of the Radiology and Medical Imaging Department with a Clinic; ORCID: 0000-0001-5008-954X; eLibrary SPIN: 1211-7685; e-mail: lukin.mv.radiology@gmail.com

Yana A. Filin, resident of the Radiology and Medical Imaging Department with a Clinic; ORCID: 0009-0009-0778-6396; e-mail: filin_yana@mail.ru

***Daniil A. Beregovskii**, resident of the Radiology and Medical Imaging Department with a Clinic; address: 2, Akkuratova st., Saint Petersburg, Russia, 197341; ORCID: 0009-0008-7964-7857; e-mail: bereg.daniil96@mail.ru

Elena D. Vyshedkevich, radiologist of the Magnetic Resonance Imaging Department; ORCID: 0000-0001-9698-1795; e-mail: vyshedkevich.ed@mail.ru

Alexander Yu. Efimtsev, MD, Dr. Sci. (Medicine), Associate Professor of the Radiology and Medical Imaging Department with the Clinic; ORCID: 0000-0003-2249-1405; eLibrary SPIN: 3459-2168; e-mail: atralf@mail.ru

Gennady E. Trufanov, MD, Dr. Sci. (Medicine), Professor, the Head of the Radiology and Medical Imaging Department with the Clinic; ORCID: 0000-0002-1611-5000; e-mail: trufanovge@mail.ru

ОБ АВТОРАХ

Лукин Максим Владимирович, аспирант кафедры лучевой диагностики и медицинской визуализации с клиникой; ORCID: 0000-0001-5008-954X; eLibrary SPIN: 1211-7685; e-mail: lukin.mv.radiology@gmail.com

Филин Яна Альбертовна, ординатор кафедры лучевой диагностики и медицинской визуализации с клиникой; ORCID: 0009-0009-0778-6396; e-mail: filin_yana@mail.ru

***Береговский Даниил Андреевич**, ординатор кафедры лучевой диагностики и медицинской визуализации с клиникой; адрес: 197341, Россия, г. Санкт-Петербург, ул. Аккуратова, д. 2; ORCID: 0009-0008-7964-7857; e-mail: bereg.daniil96@mail.ru

Вышедкевич Елена Дмитриевна, врач-рентгенолог отделения магнитно-резонансной томографии; ORCID: 0000-0001-9698-1795; e-mail: vyshedkevich.ed@mail.ru

Ефимцев Александр Юрьевич, докт. мед. наук, доцент кафедры лучевой диагностики и медицинской визуализации с клиникой; ORCID: 0000-0003-2249-1405; eLibrary SPIN: 3459-2168; e-mail: atralf@mail.ru

Труфанов Геннадий Евгеньевич, докт. мед. наук, профессор, заведующий кафедрой лучевой диагностики и медицинской визуализации с клиникой; ORCID: 0000-0002-1611-5000; e-mail: trufanovge@mail.ru

* Corresponding author / Автор, ответственный за переписку