Structural association between heterotopia and cortical lesions visualised with 7 T MRI in patients with focal epilepsy

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A B S T R A C T

Purpose: To analyze structural characteristics of malformations of cortical development (MCD) at 7T and 3T MRI.

Methods: Twenty-five patients were examined with a 7T MRI-scanner in addition to 3T examinations performed for epilepsy evaluation. 7T sequences included a 3D-T1-weighted (T1w) MPRAGE, 3D-T2w FLAIR, and heavily T2w axial and coronal high-resolution (0.5 × 0.5 × 0.75–1.0 mm³) 2D-TSE sequences. Images were reviewed for 7T MRI imaging characteristics of MCD, visibility and frequency of identified lesions on 7T and on 3T (original reports and second reading).

Results: In 25 patients 112 lesions were identified (57 gray matter (GM) heterotopia, 37 focal cortical dysplasia (FCD), and 18 other MCD). Imaging characteristics of the 37 FCD were cortical thickening (n = 11); GM-WM border blurring (n = 30); GM signal intensity changes (n = 18); juxtacortical WM signal intensity changes (n = 18); and transmantle WM signal intensity changes (n = 11). None of the 7T MRI sequences was sufficient to detect all types of lesions. Heterotopia were in general isointense to normal GM. Structural associations between 36 heterotopia and overlaying cortex were observed, composed either of a direct connection, vessel-like structures, or GM-like bridges. FCD were mentioned in 30% (11 of 37) of the original reports at 3T, and in 57% (21 of 37) after second reading. FCD connections to subcortical heterotopia were clinically not reported at all.

Conclusion: 7T MRI revealed subtle connections between heterotopia and previous unidentified pathology in overlaying cortex. These findings may be significant for the understanding of the anatomical seizure origin and propagation pathways.

1. Introduction

Drug resistant epilepsy comprises 30–40% of people suffering from focal epilepsy. High-quality imaging is crucial in the evaluation of drug resistant epilepsy patients, since as many as 50% of these patients may be potential candidates for surgical resection [1, 2]. Magnetic resonance imaging (MRI) preferably using a 3 T system is included in the pre-surgical work up for lesion detection [3]. The most important predictor for good surgical outcome is complete removal of an MRI detectable epileptogenic brain lesion [4, 5].

Focal cortical dysplasia (FCD) is the most common malformation of cortical development (MCD) in children operated for drug resistant epilepsy, and the third most common in adults, following hippocampal sclerosis and tumours [6]. FCD are histologically sub-classified, and the most important histopathological findings are for FCD I abnormal cortical lamination, for FCD IIa and IIb dysmorphic neurons with or without balloon cells, and for FCD III abnormal cortical lamination adjacent to another malformation [7]. Structural MRI findings in
different FCD include, for example, blurring of the gray-white matter junction, increased cortical thickness, altered signal intensity, localized parenchymal thinning, and the transmantle sign (seen only in FCD II) [5, 7,8]. The conspicuousness of these findings varies between different field strengths, sequences used, lesion types, lesion size, and the subtleness of the lesion itself. A challenge often encountered during the investigation of epilepsy patients is that FCD I is typically not seen on MRI, resulting in underdiagnosis of these lesions and potentially suboptimal postsurgical outcome [8].

Another frequently identified MCD during investigation of drug resistant epilepsy patients is gray matter heterotopia, a malformation due to abnormal neuronal migration and sub-classified according to location – e.g., periventricular nodular heterotopia, subcortical heterotopia and subcortical band heterotopia [9-11]. Despite the suspicion of heterotopia playing a role in epileptogenicity, only few studies have been conducted to evaluate this further, with those primarily focusing on invasive electroencephal graphical findings of the heterotopic tissue and overlaying cortex [12,13]. A DTI and fMRI-based connectivity between periventricular nodular heterotopia and overlaying cortex has been identified earlier [14] and Battaglia et al. illustrate well EEG and SEEG findings related to abnormal anatomical circuitries including heterotopic nodules and adjacent cortical areas [15].

MRI negative patients operated for drug resistant epilepsy are diagnosed with FCD in 42–73% of cases [16-18], suggesting inadequate sensitivity of standard presurgical MRI for FCD [19]. Although complete resection of the FCD is fundamental for significantly better postoperative outcome [4,5], heterotopia-associated epilepsy surgery has not shown similarly promising results [12,13,20,21], indicating a potential gap in presurgical structural assessment of the lesions and related epileptic networks. Structural characterization and detection of epileptogenic lesions, especially in drug resistant MRI negative patients, benefit from increased MRI field strength [22-28].

Therefore, the purpose of this study was to analyze structural characteristics of malformations of cortical development at ultra-high field MRI with special focus on potential structural substrates for epileptic circuitries between deep and cortical brain lesions and a comparison to findings at lower field strength.

2. Materials and methods

2.1. Study design and patient inclusion

Patients investigated for epilepsy at the Department of Neurology, Skåne University Hospital, Sweden between 2016 and 2021, including national referrals, were included in a prospective explorative cohort study evaluating MRI imaging findings in epilepsy at 7 T. In this subcohort aiming at the evaluation of MCD, the first 25 consecutive patients with one or more identified MCD lesions at 7 T were included. Exclusion criteria were pregnancy, contraindications for MRI or previous neurosurgical intervention targeting the MCD in question. The study was approved by the appropriate ethical review board (entry nos. 2016/595), all patients gave written informed consent, and the study was performed according to recommendations of the Declaration of Helsinki.

2.2. 7 T MRI image acquisition

All measurements were performed on an actively shielded 7 T MRI scanner (Philips 7 T Achieva; Philips, Best, The Netherlands), using a dual-channel transmit and 32-channel receive head coil (Nova Medical, Wilmington, Massachusetts, USA). For increased field homogeneity, dielectric pads were used during image acquisition [28]. T1-weighted (T1w) images were acquired using a sagittal, whole brain, magnetization prepared 3D fast gradient echo sequence (MPRAGE) with repetition time 8 ms, echo time 2.8 ms, flip angle 7° and isotropic 0.6 mm voxel dimensions. T2-weighted (T2w) fluid-attenuated inversion recovery (FLAIR) images were acquired using a sagittal, whole brain, 3D turbo spin echo (TSE) sequence with repetition time 6000 ms, echo time 390 ms, flip angle 55° and a spatial resolution of 0.69×0.69×1.4 mm³ (reconstructed to 0.69×0.69×0.7 mm³). Highly T2-weighted 2D coronal and axial image series were acquired using a TSE sequence with repetition time 3500 ms, echo time 60 ms and flip angle 90°. Depending on lesion size, 0.5 × 0.5 × 0.75 mm³ or 0.5 × 0.5 × 1 mm³ spatial resolution and 32 slices were used for axial images and 0.5 × 0.5 × 1 mm³ spatial resolution and 48 slices for coronal images, rendering partial brain coverage.

2.3. 7 T MRI structural lesion characterization

Image evaluation was performed on a Sectra IDS7 workstation (Sectra AB, Linköping, Sweden). Only imaging findings considered to represent MCD were evaluated in this study, excluding e.g., artifacts, unclear findings, other pathologies, and anatomical variants of no clinical relevance. As far as radiologically possible, lesions were classified according to MCD classifications [7-11]. Lesions were evaluated regarding localization in hemisphere, lobe, largest diameter, and for signal intensity (T1w, T2w and FLAIR) compared to normal white matter (WM) and/or normal gray matter (GM) (hyperintense, iso-intense, hypointense). Heterotopia were further evaluated for presence and type of connection to cortex or cortical lesions (clear, subtle, no connection) and type of associated cortical lesion if present. FCD and other cortical MCD were – separately for T1w, T2w and FLAIR images – further evaluated for abnormal sulcal or gyral pattern, cortical thickening and cortical thinning, blurring of GM-WM border, subcortical WM volume loss, juxtacortical WM signal intensity change (score: clear, subtle, or not present), and transmantle WM signal changes (score: clear partial, subtle partial, clear, or subtle complete transmantle sign, or not present).

Imaging data presented in this study are consensus reading data comprising the following image evaluation steps: A primary clinical reading of the 7 T images by a clinical neuroradiologist and reviewed during specialized multidisciplinary (MDC) epilepsy conferences was performed and documented in the radiological information system. Image interpretation for this study was performed by one of the authors (IBM), a neuroradiologist with more than 20 years of experience and a special interest in epilepsy. The findings from this secondary expert reading were compared to the primary clinical reading. Findings not reported earlier were added to the patient journal and a consensus reading with another experienced clinical neuroradiologist was performed if necessary.

2.4. Comparison 7 T versus 3 T MRI

Clinical 3 T MRI examinations previously performed with dedicated epilepsy protocols could be retrieved for comparison for all patients except one. As these examinations were performed at different hospitals and on different scanners, examination parameters differed and are not listed for the individual cases. A prerequisite for inclusion of 3 T MRI examinations was availability of 3D T1w, 2D T2w (at least one plane) and/or true inversion recovery (IR) T1w (coronal and/or axial), and 3D FLAIR and/or 2D FLAIR (the latter with a slice thickness ≤ 3 mm) images. In a second reading by the same reviewer as the 7 T material (IBM), 3 T MRI images were evaluated for the presence of lesions (MCD and connections between heterotopia and cortex/cortex pathology) as identified at 7 T (yes, no). Findings from the second reading were compared to original 3 T reports and MDC epilepsy conference notes covering the 3 T MRI examinations in question (discordant findings, lesion not earlier reported). Lesion characterization for different sequences as performed for 7 T was not conducted and is not within the scope of this paper, as the 3 T image material was evaluated retrospectively and was heterogeneous regarding MR systems (not field strengths) and consequently sequence parameters used.
3. Results

3.1. 7 T MRI structural lesion characterisation

The 25 patients (mean age 30 years, range 14 to 53; 11 males) had a total number of 112 MCD; 57 heterotopia (Table 1, Fig. 1), 37 FCD (Table 2, Fig. 2) and 18 other MCD (eight polymicrogyria, six polymicrogyria combined with incomplete schizencephaly, and four pachygyria combined with incomplete lissencephaly).

3.1.1. Heterotopia

Among heterotopia, periventricular nodular (24 lesions in eight patients) and subcortical nodular and/or curvilinear heterotopia (25 lesions in six patients) were most common, while bilateral bandheterotopia (8 lesions) were seen in two patients.

Imaging characteristics are summarized in Table 1. Heterotopia were in general easily identified as signal intensity was comparable to GM signal in 100% of lesions in T1w images, 92% of lesions in T2w images and 81% of lesions in FLAIR images. Two bandheterotropias were iso-intense to WM on T2w and FLAIR images, thus only adequately detectable on T1w images.

Structural connections to cortex or cortical pathology by pronounced vessel structures, GM bridges, and/or direct contact were seen in 23 (96%) periventricular heterotopia and 13 (52%) subcortical heterotopia (Table 1, Fig. 1, Fig. 3). FCD were most common among lesions associated to these heterotopia (Table 1). One of these cases where histopathology confirmed the presence of suspected pathologic changes in the cortex overlaying the heterotopia is illustrated in Fig. 3.

3.1.2. Focal cortical dysplasia

Imaging characteristics of the 37 FCD are summarized in Table 2 and illustrated in Fig. 2. Visually appreciable imaging characteristics seen in at least one sequence were: cortical thickening in 11 FCD (30%); blurring of the GM-WM border in 30 FCD (81%); signal intensity changes within the affected GM in 18 FCD (49%); juxtacortical WM signal changes in 18 FCD (49%); and transmantle WM signal changes in 11 FCD (30%). This results in 171 positive findings regarding the before mentioned imaging characteristics for the three evaluated sequences, and 65% of these findings were subtle. None of the evaluated sequences or evaluated lesion characteristics could stand alone for the detection of all lesions.

3.1.3. Other malformations of cortical development

Other malformations of cortical development included four patients with polymicrogyria, one patient with polymicrogyria and incomplete schizencephaly, and one patient with pachygyria combined with incomplete lissencephaly. Main lesion characteristics for the 18 lesions in these patients were: cortical thickening (n = 12), GM-WM blurring (n = 6), subcortical WM volume loss (n = 11). More detailed imaging characteristics are given in Supplementary Table 1.

### Table 1

| Lesion characteristics | Periventricular nodular heterotopia | Subcortical heterotopia nodular | Curvilinear | Mixed nodular &curvilinear | Band heterotopia |
|------------------------|------------------------------------|-------------------------------|-------------|---------------------------|-----------------|
| **Patients, n**        | 8                                  | 4                             | 1           | 2                         | 2               |
| **7 T evaluation**     |                                    |                               |             |                           |                 |
| Lesions, n             | 24                                 | 11                            | 9           | 5                         | 8               |
| Side, n right; n left  | 11; 13                             | 6; 5                          | 5; 4        | 4; 1                      | 4: 4            |
| Affected lobes, n (per lobe/s) | 7 (T; TO); 5 (P; 1 (F, O, P, PTT, FFPO) | 10 (F; 1 (I) | 9 (F) | 4 (F); 1 (PO) | 2 (F, PTO); 4 (PPTO) |
| **Size** (mean cm, range) | 2.4 (0.5–7)                     | 1.2 (0.5–3.5)                 | 0.6 (0.5–1) | 3 (1–6) | NA*              |
| MR signal isointense compared to normal GM, n lesions (%) | 24 (100%) | 11 (100%) | 9 (100%) | 5 (100%) | 8 (100%) |
| [other signal intensities, n lesions] | 22 (92%) | 8 (89%)* | 8 (100%)* | 5 (100%) | 6 (75%) |
| FLAIR                  | 19 (79%)                           | 8 (73%)                       | 8 (89%) | 4 (80%) | 6 (75%) |
| [hypointense to GM]    | 15 (62%)                           | 3 (22%)                       | 2 (22%) | 1 (0%) | 2 (25%) |
| Hyperintense to cortex/cortical pathology, n (%) | 23 (96%) | 6 (55%) | 2 (22%) | 5 (100%) | 0 (0%) |
| Connection between heterotopia and cortex/cortical pathology | 8, V, FCD | 4, V, FCD | 2, GMB+DC, FCD | 3, GMB+V, FCD | 8, no connection, MCDc |
| n heterotopia, type of connection, type of associated cortical lesion if present | 3, V, PMG | 2, GMB+DC, FCD | 2, DC, MCDb | 8, no connection, MCDc |
| **3 T evaluation, second reading** | 22*** | 9*** | 9 | 5 | 8 |
| Lesions, n             | 18 (82%)                           | 4 (44%)                       | 2 (22%) | 5 (100%) | 0 (0%) |
| Heterotopia with connection to cortex/cortical pathology, n (%) | 3, V, PMG | 1, V, no lesion | 2, GMB+DC, FCD | 3, GMB, FCD | 8, no connection, MCDc |
| n heterotopia, type of connection, type of associated cortical lesion if present | 3, GMB, FCD | 2, no lesion | 2, DC, MCDb | 8, no connection, MCDc |

*not applicable as long, thin bands underlie cortex over large areas, which makes it imprecise to measure a largest diameter. ** missing data in two nodular and one curvilinear subcortical heterotopia, which were not covered by the high resolution T2-weighted images with limited brain coverage. *** patient had 3 T images that could not be retrieved for second reading (2 nodular and 2 periventricular heterotopia); DC, direct contact; F, frontal lobe; FCD, focal cortical dysplasia; GM, gray matter; GMB, GM bridge connection; I, insula; MCD, malformation of cortical development; MCDa, polymicrogyria and incomplete schizencephaly (n = 4), polymicrogyria (n = 3); MCDb, polymicrogyria and incomplete schizencephaly; MCDc, incomplete lissencephaly och pachygyria; O, occipital lobe; P, parietal lobe; PMG, polymicrogyria; T, Temporal lobe; V, vessel WM, white matter.
3.2. Comparison between 7 T MRI reading, 3 T MRI second reading, and 3 T original reports and MDC reports

Among FCD identified at 7 T (n = 37), 57% (n = 21) could also be found during the second reading of the 3 T images while only 30% (n = 11) were mentioned in the original 3 T MRI reports or in reports of MDC conferences focusing on epilepsy (Table 3). FCD not identified during the second reading of the 3 T material were primarily found in cases with heterotopia, especially periventricular heterotopia, and structural connections to pathologic cortical tissue at 7 T. Heterotopia and other MCD identified at 7 T were identified during the 3 T second reading and reported in original reports or epilepsy conferences with

Table 2

| Lesions, n total (n clear; n small or subtle) | 37 (21; 16) |
| Side (right), n lesions | 22 |
| Lobes affected, n lesions per lobe/s | 14 F; 5 P; 8 T; 1 O; 2 FPT; 1 PT; 6 TO |
| Size, mean cm (range) | 1.5 (0.5–5) |
| Abnormal sulcal or gyral pattern, n total (n clear; n subtle) | 10 (6; 4) |
| Subcortical WM volume loss, n total (n clear; n subtle) | 15 (6; 9) |

| Cortical thickening | GM-WM blurring | Signal hyperintensity compared to normal GM (hypointensity, n = 0) | Juxtacortical WM signal hyperintensity (↑) or hypointensity (↓) | Transmantle WM signal hyperintensity (↑) or hypointensity (↓) |
|---------------------|----------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| T1w 8 (0; 8) | 29 (6; 23) | 1 (0; 1) | ↓ 11 (3; 8) | ↓ 6 (1; 1; 2) |
| T2w 8 (0; 8) | 17 (8; 9) | 14 (3; 11) | ↑ 14 (9; 5) ** | ↑ 7 (2; 2; 3) |
| FLAIR 7 (1; 6) | 15 (5; 10) | 15 (4; 11) | ↑ 11 (7; 4) | ↑ 7 (2; 2; 3; 0) |
| Total 11 | 30 | 18 | 18 | 11 |

* Four lesions missing as lesions are not covered by sequence; **One lesion missing as lesion is not covered by sequence; F, frontal; FLAIR, fluid attenuation inversion recovery; GM, gray matter; O, occipital; P, parietal; T, temporal; T1w, T1-weighted; T2w, T2-weighted; WM, white matter.
few exceptions (Table 1 and Table 3).

4. Discussion

This study explores ultra-high field imaging characteristics of MCD in people with epilepsy and reveals structural findings that may represent the substrate for earlier reported epileptic circuitries and functional connectivity between heterotopia and cortical brain lesions. Our most important finding regarding lesion characterization was an association between predominantly periventricular heterotopia and adjacent cortex (Fig. 3) - best described as signal changes in the white matter resembling gray matter bridges, loss of white matter leading to the proximity of the heterotopia and cortical structures or pronounced vessel structures. A structural association between heterotopia and gray matter has previously been suspected and described in functional studies [14, 22–24]. It is in line with earlier indications from histological, genetical and electroencephalographic reports [29–31] regarding a connection between periventricular heterotopia and adjacent cortex (Fig. 3) - best described as signal changes in the white matter resembling gray matter bridges, loss of white matter leading to the proximity of the heterotopia and cortical structures or pronounced vessel structures.

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With the guidance of 7 T imaging, the association was partially seen even using lower field strength. The incidence of these findings in our material is intriguing as well as the fact that FCD were most often suspected as associated lesions, explaining heterotopia’s active role in hyperexcitability by establishing an epileptic network with the overlaying cortex. The intrinsic epileptogenicity in FCD is undisputed [5,32], but the same does not yet apply for heterotopia. Already in the 1990’s several studies showed controversial results concerning the arousal of epileptogenic activity directly from the heterotopic nodules of periventricular nodular heterotopia [12,21]. Later studies [13,20,30] confirmed epileptic discharges in periventricular heterotopia and in association with polymicrogyria, although they often could not elucidate their role in the initiation of seizures, as they observed a simultaneous ictal onset within the heterotopia and the overlaying cortex, and thus leaving heterotopia’s role in epileptogenesis still unclear.

Even though the epileptogenic networks have been widely discussed and accepted, many questions remain concerning their visualization. Based on our findings, 7 T MRI may offer new knowledge in this context that might also be translated to lower field strength. As illustrated with a case verified by histopathology, this paper directs our interest towards the potential importance of MRI to identify pathologic cortical areas overlaying heterotopia in the evaluation of potential epileptogenic foci. The fact that many of these subtle findings were subsequently identified in 3 T examinations during re-assessment, consequently, underlines the significance of a detailed visual interpretation during a pre-surgical evaluation. Furthermore, high resolution imaging with partial brain coverage focusing on cortical areas overlaying heterotopia is feasible also on 3 T MRI systems with heavily T2-weighted sequences within reasonable acquisition times. Most qualified epilepsy centres dispose of access to 3 T MRI scanners, while 7 T scanners are less accessible. During the presurgical evaluation of epilepsy cases with heterotopia as isolated finding, careful attention should be paid to the surrounding tissue and overlaying cortex.

In clinical routine, a protocol comprising different MRI sequences is recommended for evaluation of epilepsy patients [2] and the set used in this study (T1w, T2w and FLAIR images) showed individual strengths regarding specific image characteristics, however, none of the sequences was superior to the other two, even when considering different imaging characteristics separately.

We allowed a considerable heterogeneity of our cohort extending inclusion to any type of MCD present to increase lesion numbers, decreasing selection bias, and reflecting a true clinical context for this patient group. However this study focused on structural sequences

Fig. 2. Focal cortical dysplasia illustrated in two cases (case #1 upper row and case #2 lower row) with T1-weighted (T1w) images (left), T2w images (middle) and FLAIR images (right). Lesions are marked in T1w images. Appreciable imaging characteristics are cortical thickening, blurring of the gray matter (GM)-white matter (WM) border, signal intensity changes within the affected GM and in juxtacortical WM, and transmantle WM signal changes, the latter only in the upper row. Note the distinct T2 hyperintensity in the juxtacortical WM.
accessible for clinical visual interpretation, consciously avoiding advanced post-processing [33] or advanced functional MRI techniques necessitating post-processing not available in clinical routine [34]. Although originating from different sites, MR examinations at 3 T were only included and evaluated if performed according to an epilepsy protocol, including at least a subset of specific sequences, and primarily read considering an epilepsy evaluation. Further all examinations underwent a second reading with 7 T MR findings known to evaluate the presence of known lesions rather than to evaluate a reader’s ability to identify lesions.

5. Conclusion

We were able to visualize subtle connections between heterotopic tissue and overlaying cortex, as well as pathology in these cortical areas. This is confirmative with previous functional findings, and indicative of heterotopia’s epileptogenicity. Visual interpretation strategies of clinical MRI images in people with epilepsy and heterotopia in particular
might, in the light of 7 T MRI lesion characteristics identified for MCD in this study, need reappraisal.

Author contributions

AZ: study conduction, data analysis, writing and revision of the manuscript.

BH: study conduction and revision of the manuscript.

KMB: study design and revision of the manuscript.

EE: data analysis and revision of the manuscript.

KK: study design and revision of the manuscript.

MCS: study design and data analysis, writing and revision of the manuscript.

IBB: study design and data analysis, writing and revision of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found in the online version, at doi:10.1016/j.seizure.2022.08.008.

References

[1] Engel Jr J. The current place of epilepsy surgery. Curr Opin Neurol 2018;31(2):192-7.

[2] Opheim G, van der Kolk A, Markenroth Bloch K, Colon AJ, Davis KA, Henry TR, et al. 7T Epilepsy Task Force Consensus Recommendations on the Use of 7T MRI in Clinical Practice. Neurology 2021;96(7):327-41.

[3] Basnagartner C, Koren JP, Brito-Arias M, Zochle L, Firker S. Presurgical epilepsy evaluation and epilepsy surgery. F1000Res 2019;8.

[4] Krsek P, Maton B, Jayakar P, Dean P, Korman B, Rey G, et al. Incomplete resection of focal cortical dysplasia is the main predictor of poor postsurgical outcome. Neurology 2009;72(3):217-23.

[5] Lee SK, Kim DW. Focal cortical dysplasia and epilepsy surgery. J Epilepsy Res 2013;3(2):43-7.

[6] Blumcke I, Spreafico R, Hauker G, Coras R, Kobow K, Bien CG, et al. Histopathological Findings in Brain Tissue Obtained during Epilepsy Surgery. N Engl J Med 2017;377(17):1648-56.

[7] Najm IM, Sarnai HB, Blumcke I. Review: the international consensus classification of Focal Cortical Dysplasia - a critical update 2018. Neuropathol Appl Neurobiol 2018;44(1):18-31.

[8] Colombo N, Salamon N, Raybaud C, Ozdara C, Barkovich AJ. Imaging of malformations of cortical development. Epileptic Disord 2009;11(3):194-205.

[9] Barkovich AJ, Guerrini R, Kuzniecky RI, Jackson GD, DoByn WB, A developmental and genetic classification for malformations of cortical development: update 2012. Brain 2012;135(Pt 5):1348-69.

[10] Barkovich AJ, Kuzniecky RI. Gray matter heterotopia. Neurology 2000;55(11):1603-8.

[11] Oegema R, Barkovich AJ, Mancini GMS, Guerrini R, DoByn WB. Subcortical heterotopic gray matter brain malformations: classification study of 107 individuals. Neurology 2019;93(14):e1360-e73.

[12] Koibare SV, VmLandingham K, Arrows C, Luther JS, Friedman A, R一千ke RA. Seizure onset from periventricular nodular heterotopias: depth-electrode study. Neurology 1998;51(6):1723-7.

[13] Tassi L, Colombo N, Gossu M, Mai R, Franscione S, G Lo Russo, et al. Electroclinical, MRI and neuropathological study of 10 patients with nodular heterotopia, with surgical outcomes. Brain 2005;128(Pt 2):321-37.

[14] Christodoulou JA, Walker LM, Del Tufo SN, Katriz T, Gabrielli JD, Whitfield-Gabrielli S, et al. Abnormal structural and functional brain connectivity in gray matter heterotopia. Epilepsia 2012;53(6):1024-32.

[15] Battaglia G, Chiapparini L, Franchecchetti S, Frei E, Tassi L, Bassanini S, et al. Periventricular nodular heterotopia: classification, epileptic history, and genesis of epileptic discharges. Epilepsia 2006;47(1):86-97.

[16] Chapman K, Wylie E, Najm I, Ruperti F, Bingaman W, Luders J, et al. Seizure outcome after epilepsy surgery in patients with normal preoperative MRI. J Neurol Neurosurg Psychiatry 2005;76(5):710-3.

[17] Lee SK, Lee SY, Kim KK, Hong KS, Lee DS, Chung CK. Surgical outcome and prognostic factors of cryptogenic neocortical epilepsy. Ann Neurol 2005;58(4):525-32.

[18] McGonigal A, Bartolomei F, Regis J, Gaye M, Gavaret M, Trebuchon-Da Fonseca A, et al. Stereoelectroencephalography in presurgical assessment of MRI-negative epilepsy. Brain 2007;130(Pt 12):3169-83.

[19] Duncan JS, Winston GP, Koepf MJ. 3D surface rendering in the assessment for epilepsy surgery. Lancet Neurol 2016;15(4):420-33.

[20] Aghakhani Y, Kiny D, Gotman J, Samal M, Ouellette P, Olivier A, et al. The role of periventricular nodular heterotopia in epileptogenesis. Brain 2005;128(3):641-51.

[21] DuBose F, Tampieri D, Lee N, Andermann E, Carpenter S, Leblanc R, et al. Periventricular and subcortical nodular heterotopia. A study of 33 patients. Brain 1995;118(Pt 5):1273-87.

[22] Boulougne S, Pizzo F, Chatard B, Roehri N, Catenoix H, Ostrowsky-Coste K, et al. Functional connectivity and epileptogenieity of nodular heterotopia: a single-pulse stimulation study. Epilepsia 2021;1-13.

[23] Christodoulou JA, Bansard ME, Del Tufo SN, Katriz T, Whitfield-Gabrielli S, Gabrielli JD, et al. Integration of gray matter nodules into functional cortical circuits in periventricular heterotopia. Epilepsy Behav 2013;29(2):400-6.

[24] Deleo F, Hong SJ, Fadade F, Caldaireau B, Krulsk B, Bernasconi N, et al. Whole-brain multimodal MRI phenotyping of periventricular nodular heterotopia. Neurology 2020;95(17):e2418-e26.

[25] Knake S, Siantaffyliou C, Wull LL, Wiggins G, Kirk GP, Larson PG, et al. 3T phased array MRI improves the presurgical evaluation in focal epilepsies: a prospective study. Neurology 2005;65(7):1026-31.

[26] Phal FM, Usmanov A, Nesbit GM, Anderson JC, Spencer D, Wang P, et al. Qualitative comparison of 3-T and 1.5-T MRI in the evaluation of epilepsy. AJR Am J Roentgenol 2008;191(3):890-5.

[27] Strandberg M, Larson EM, Backman S, Kallsen K. Pre-surgical epilepsy evaluation using 3T MRI. Do surface coils provide additional information? Epileptic Disord 2008;10(2):83-92.

[28] Trouwisse WM, Brink WM, Webb AG. Quantitative assessment of the effects of high-permittivity pads in 7 Tesla MRI of the brain. Magn Reson Med 2012;67(5):1285-93.

[29] Guerrini R, DoByn WB. Malformations of cortical development: clinical features and genetic causes. Lancet Neurol 2014;13(7):710-26.

[30] Pizzo F, Roehri N, Catenoix H, Medina S, McGonigal A, Giubiano B, et al. Epileptogenic networks in nodular heterotopia: a stereoelectroencephalography study. Epilepsia 2017;58(12):2112-23.

[31] Wiuck G, Leventer RJ, Squier WM, Jansen A, Andermann E, DuBose F, et al. Periventricular nodular heterotopia with overlying polymicrogyria. Brain 2005;128(Pt 2):321.

[32] Fuess S, Essang C, Altenmuller DM, Stack AM, Steinhoff BJ, Strobl K, et al. Long-term seizure outcome in 211 patients with focal cortical dysplasia. Epilepsia 2015;56(1):66-76.

[33] Wang I, Oh S, Blumcke I, Coras R, Krishnan B, Kim S, et al. Value of 7T MRI and post-processing in patients with nonlesional 3T MRI undergoing epilepsy presurgical evaluation. Epilepsia 2020;61(11):2509-20.

[34] Lampinen B, Zampeli A, Bjorkman-Burtscher IM, Szczepankiewicz F, Kallen K, Compagnone Strandberg M, et al. Tensor-valued diffusion MRI differentiates cortex and white matter in malformations of cortical development associated with epilepsy. Epilepsia 2005;46(8):1701-12.