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Neurogenic heterotopic ossification of the hip: Magnetic resonance imaging versus computed tomography for pre-surgical assessment

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ABSTRACT

Purpose: Neurogenic heterotopic ossification (NHO) of the hip is a frequent complication of spinal cord injuries, often requiring surgical management. Pre-surgical imaging assessment is essential, usually with computed tomography (CT)-scan. We aimed to compare magnetic resonance imaging (MRI) and CT for pre-surgical imaging assessment of the NHO, particularly for their relationships with vessels and nerves.

Method: This prospective study included consecutive patients who underwent surgery for NHO from July 2019 to April 2022. All patients had CT angiography and MRI including Zero Echo Time and TRICKS sequences. Radiologists used standardized reports for CT and MRI to evaluate NHO and their features, bone mineralization, and relation to the arteries, veins and nerves. Agreement between pre-surgical CT and MRI was evaluated.

Results: Twenty-four patients (mean age: 53.5 ± 12.2 years) were included, among which 7 had bilateral NHO (31 hips). NHO were anterior in 15/31 hips (48 %), multifragmented in 25/31 hips (81 %). Mild and significant demineralization was most frequent. Gutter and tunnel were reported in 11.1 % of the arteries. Nerves were more often identified in MRI than in CT-scan. Agreement coefficients between CT and MRI were excellent for NHO location (0.95) and implantation (0.92), good for fragmentation (0.70), contact with joint capsule (0.66), bone mineralization (0.74), and relation to arteries (0.85), veins (0.76), sciatic nerve (0.7) and moderate for femoral nerve (0.47).

Conclusion: MRI exhibited a good agreement with CT for pre-surgical assessment of NHO of the hip, especially to evaluate their relationships with the arteries, veins and sciatic nerve. Femoral nerves were more often identified in MRI than in CT-scan.

1. Introduction

Neurogenic heterotopic ossification (NHO) of the hip, also called neurogenic *para*-osteoarthropathy, is a frequent complication of central nervous system injuries, occurring in approximately 20–25 % of patients after traumatic spinal cord injury [1–3], characterized by the development of heterotopic ossifications in *peri*-articular soft tissues, sometimes

with vessels or nerves compressions. The pathophysiology is complex and incompletely understood. Metabolic and vascular changes occur due to prolonged immobilization and autonomic dysregulation, followed by inflammation and hypoxia leading to increasing growth factor activity and osteoblasts developing ectopic bone matrix [4,5]. Surgical management is complex and requires pre-surgical imaging assessment to prevent intra-operative and post-surgical complications, such as

Abbreviations: CT, Computed Tomography; MRI, Magnetic Resonance Imaging; NHO, Neurogenic heterotopic ossification; STIR, Short-tau inversion recovery; ZTE, Zero Echo Time.

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Table 1
Patients' characteristics.

	Number (%)
Sex	
Male	21/24 (87.5 %)
Female	3/24 (12.5 %)
Age (years) ¹	53.5 ± 12.2
Etiology	
Brain trauma	3/24 (12.5 %)
Spinal cord injury	9/24 (37.5 %)
Stroke	2/24 (8.3 %)
Prolonged coma	4/24 (16.7 %)
No cause found	1/24 (4.2 %)
Unknown	5/24 (20.8 %)
Hip	
Right	11/24 (46 %)
Left	6/24 (25 %)
Bilateral	7/24 (29 %)

¹ Ages are reported as mean ± standard deviation

hemorrhages or nerve injuries [6,7].

Computed tomography (CT) angiography with iodinated contrast injection is currently the gold standard for pre-surgical imaging assessment, providing high resolution and excellent contrast for vessels [8]. CT-scan provides NHO cartography and evaluation of its relationships with vessels and nerves [9].

Cortical bone, which exhibits a low proton density, has a relaxation time too short to be analyzed with conventional MRI sequences. Zero Echo Time (ZTE) sequence has been developed to acquire images with an echo time of as low as a few microseconds after radiofrequency excitation pulse and provides excellent osseous contrast [10], e.g. for imaging of the shoulder [11] or evaluation of cervical neural foraminal stenosis [12]. An excellent agreement has also been reported between MRI and CT-scan for the evaluation of NHO features in a previous preliminary study that included some patients of this study [13]. However, pre-surgical imaging of NHO requires cautious vascular and nervous analysis, which could be performed with MRI instead of CT-scan.

We aimed to compare the performances of MRI and CT-scan for pre-surgical assessment of NHO of the hip, particularly to evaluate their relationships with the vessels and nerves.

2. Materials and methods

This single-center prospective study included consecutive patients

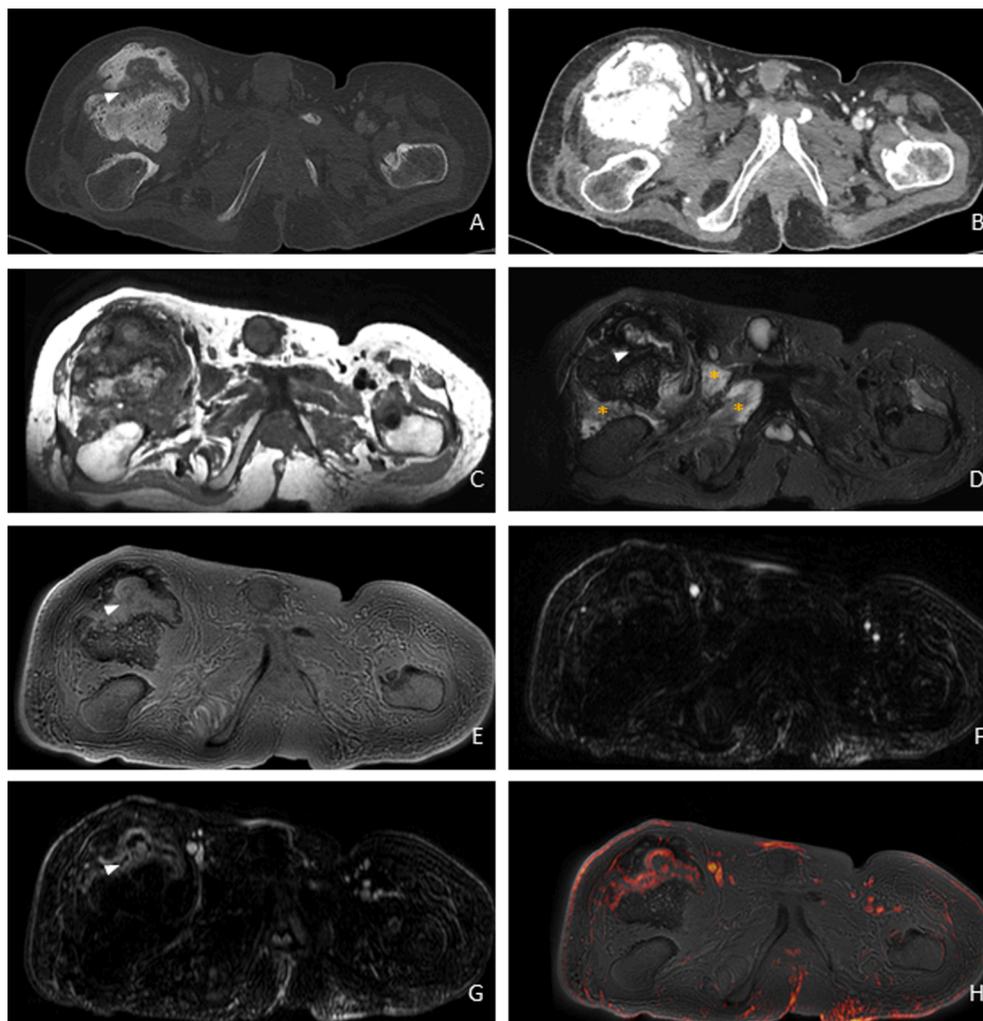


Fig. 1. Anterior multifragmented anterior NHO of the right hip. Axial images on CT in osseous (A) and soft tissues (B) windows, on T1-weighted (C), STIR (D), ZTE sequence (E), arterial phase and venous phase on TRICKS sequence (F and G), and superposition of ZTE and TRICKS sequences (H). Note the immature component of the NHO in hypersignal STIR and enhanced at the venous phase (arrowhead). Note the important denervation oedema of adductors and quadriceps muscles (*).

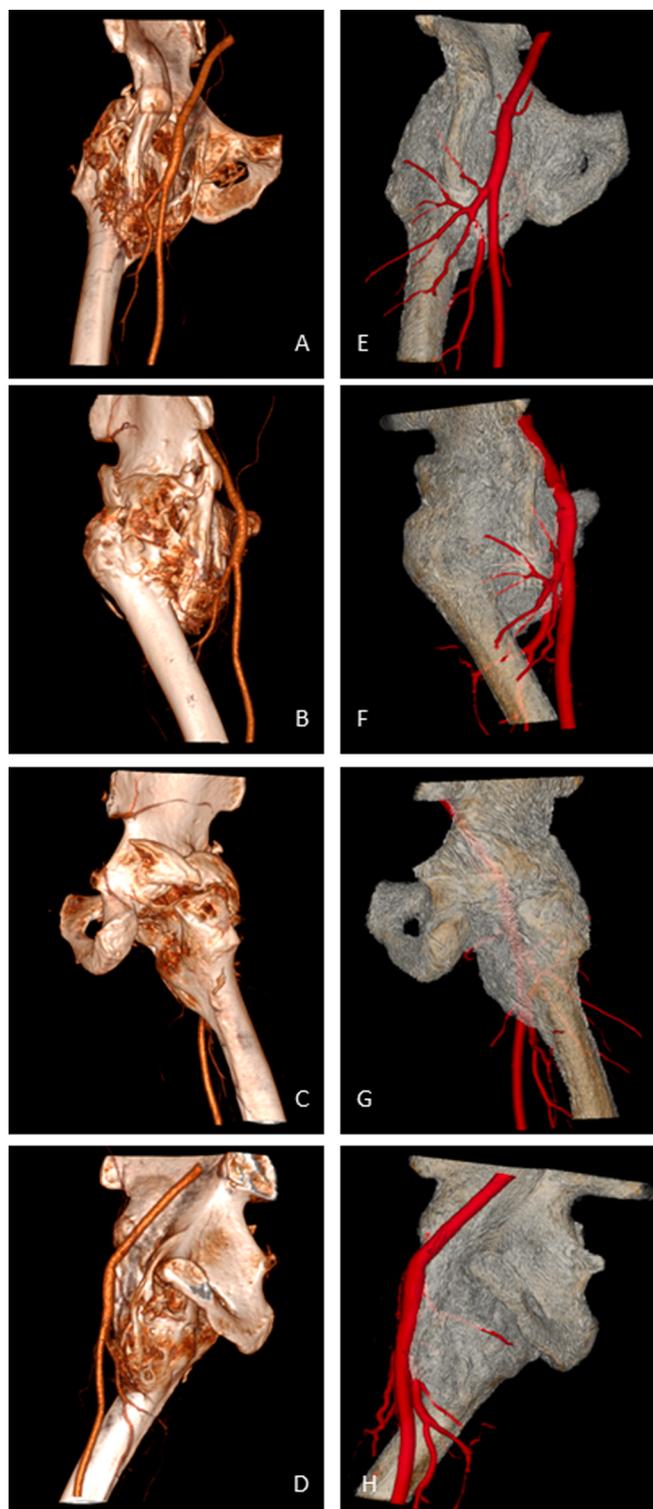


Fig. 2. 3D Volumetric rendering of an anterior monofragmentary NHO of the right hip. on CT (A–D) and MRI (E–H) at arterial phase.

who underwent surgery for symptomatic NHO of the hip in Raymond Poincaré hospital (APHP, Garches, France) from July 1st 2019 to April 30th 2022. Institutional review board approval was obtained (CPP Ile-de-France III – 3667-RM) and all patients gave informed consent to participate.

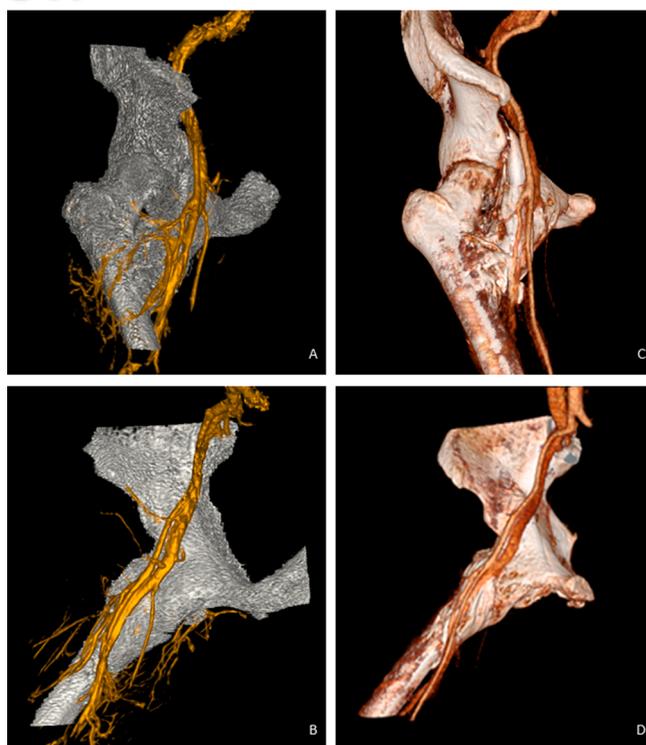


Fig. 3. 3D Volumetric rendering of an anterior NHO of the right hip. on MRI (A and B) and CT (C and D) at a biphasic arterial and venous phase.

2.1. Inclusion criteria

All patients over 18 years old with NHO of the hip due to central nervous system injury, brain or spinal cord trauma, with functional limitations for daily activity requiring surgical management were included. Surgical indication for partial or total excision of heterotopic ossifications was discussed during multidisciplinary meetings with an orthopedic surgeon and a specialist in physical and rehabilitation medicine. Patients with contra-indication to CT or MRI or contra-indication to iodinated contrast agents, such as renal disease or a history of reactions to contrast agents were excluded. Written consent was collected for all patients.

Seven patients included in this study were also included in a previous preliminary study for assessment of NHO features [13].

2.2. CT-scan technique

CT-scan was performed with a scanner (SOMATOM Definition AS, Siemens Healthineers). As previously described [9,13], one acquisition after a biphasic iodinated solution injection (iomeprol, Iomeron 400 mg/ml, Bracco Imaging) including a first injection of 120 ml at the rate of 1.5 ml/s immediately followed by a second injection of 80 ml at the rate of 3 ml/s was performed with a collimation of 128×0.625 mm and was triggered 135 s after the start of injection.

Multiplanar reconstructions were performed as well as bone and vessels volume rendering 3D images.

2.3. MRI technique

Patient positioning was crucial for this examination in order to avoid any movement of the patient. MRI was performed with a 3-T MR system (Discovery™ MR750 3.0 T, General Electrics). As previously described [13], the protocol included 3D coronal spin-echo T1-weighted, 3D axial spin-echo STIR and 3D axial ZTE sequences.

For vascular analysis, a 3D coronal TRICKS sequence (FOV = 50.0,

Table 2
Characteristics of the 31 NHO.

	Number (%)
Location	
Anterior	22/31 (71 %)
Posterior	16/31 (52 %)
Inferior	11/31 (35 %)
External	3/31 (10 %)
Circumferential extension	7/31 (23 %)
Implantation	
Anterior border of the ilium	19/31 (61 %)
Gluteal surface of the ilium	13/31 (42 %)
Ilio-pubic branch	12/31 (39 %)
Ischio-pubic branch	6/31 (19 %)
Greater trochanter	12/31 (39 %)
Lesser trochanter	16/31 (52 %)
Femoral diaphysis	18/31 (58 %)
Fragmentation	
Monofragmentary	6/31 (19 %)
Multifragmentary	25/31 (81 %)
Pseudarthrosis	20/31 (65 %)
Relation to joint capsule	
No involvement	3/31 (10 %)
Contact	24/31 (77 %)
Disruption	4/31 (13 %)
Bone mineralization	
Normal (M1)	5/31 (16 %)
Mild demineralization (M2)	13/31 (42 %)
Significant demineralization (M3)	11/31 (35.5 %)
Severe demineralization (M4)	2/31 (6.5 %)
Femoral neck fracture	0/31 (0 %)
Osteonecrosis of the femoral head	2/31 (6.5 %)

pixel size = $1.2 \times 1.6 \text{ mm}^2$, slice thickness = 3 mm, frequency = 416, phase = 320, Flip angle = 30° , BW = 62,5 kHz, phases = 30) after injection of gadolinium contrast agent (gadoteric acid, Dotarem, Guerbet) was added, allowing analysis at arterial time and at a venous time.

Multiplanar and 3D volumic reconstructions, including fusion of ZTE and TRICKS sequences, were obtained with an Advantage Windows workstation v4.6 (General Electrics).

2.4. Data reports

CT and MRI were reviewed by a fellowship-trained radiologist with 5 years of experience in pre-surgical NHO evaluation. A minimum washout period of 1 month was used between the evaluation of CT-scan images and the one of MRI. Standardized reports were completed for both CT and MRI for all patients. For each NHO, locations, circumferential extension, implantations, fragmentation and eventual pseudarthrosis (neo-joint between fragments), and relation to joint capsule were analyzed.

To appreciate the risk of a femoral neck fracture, qualitative evaluation of bone mineralization of the femoral head was also depicted and classified into four categories, using a classification based on trabecular bone density of the femoral head as previously described [8,9] and a corresponding classification based on signal intensity of the femoral head on T1-weighted and its trabecular bone density on ZTE sequence [13]: normal (M1), mild demineralization (M2), significant demineralization (M3) and severe demineralization, with a replacement of osseous tissue by fatty tissue (M4).

Femoral neck fracture or osteonecrosis of the femoral head were reported if necessary.

Relationships with the vessels around the hip were classified either as a contact, a slight displacement, a gutter or a tunnel. For each hip, five arteries and two veins were studied: the common femoral artery, the superficial femoral artery, the deep femoral artery, the medial circumflex femoral artery and the lateral circumflex femoral artery; the superficial femoral vein and the common femoral vein. Permeability or thrombosis were also reported.

Relationships with the femoral and sciatic nerves were also evaluated, when identified, and then classified (contact, slight displacement, gutter or tunnel). Imaging features of nerve compression including muscle edema were reported if necessary.

2.5. Statistical analysis

For population description, ages are reported as “means \pm standard deviation” and their ranges. The time between pre-surgical CT and MRI imaging are reported as median and interquartile range.

Qualitative variables are described by their number and percentage.

Agreement between pre-surgical CT and MRI was evaluated using Gwet’s agreement coefficient and its p-value for binary qualitative variables and using Kendall’s coefficient of concordance and its p-value for ordinal qualitative variables and quantitative variables. A coefficient < 0.20 was considered a poor agreement, from 0.21 to 0.40 a fair agreement, from 0.41 to 0.60 a moderate agreement, from 0.61 to 0.80 a good agreement and from 0.81 to 1.00 a very good agreement.

3. Results

3.1. Population/epidemiology

A total of 24 patients with functional limitations for daily activity because of NHO of the hip were included for surgical resection. Their ages ranged from 32 to 70 (mean = $53,50 \pm 12,18$ years). NHOs were bilateral in 7 patients (29,2%), representing a total of 31 hips analyzed. Patients’ characteristics are described in Table 1.

The median period between CT and MRI was 2 days (0;71).

3.2. Analysis of the NHO

NHO location was anterior only in 15 hips and posterior only in 9 hips. A circumferential extension (anterior, posterior, and inferior or external) was found in 7 hips. The most frequent implantations were the anterior border of the ilium (19 hips), the lesser trochanter (16 hips) and the femoral diaphysis (18 hips). They were multifragmented in 25 hips. Pseudarthrosis was reported in 20 hips.

A contact between heterotopic ossifications and joint capsule was found in 24 hips, with a disruption in 4 hips. No patient had coxo-femoral joint ankylosis.

Bone mineralization was studied as well on CT as on MRI. Bone mineralization was normal (M1) in 5 hips. A mild demineralization (M2) was reported the most frequently, in 13 hips. Significant mineralization (M3) was found in 11 hips, and severe demineralization (M4) in 2 hips.

Osteonecrosis of the femoral head was reported in 2 hips with NHO, diagnosed both on MRI and CT. No patient exhibited a femoral neck fracture.

Visually, NHO and their 3D volumetric views appeared to be similar in both CTA and MRA (Figs. 1–3).

Data are summarized in Table 2.

3.3. Relationships to arteries and veins

All five arteries were evaluated in all patients, excepted in a patient in which the medial and lateral circumflex femoral arteries were not enough opacified to be analyzed. 3D volumic reconstructions were realized in both CTA and MRA if necessary.

All the arteries studied were permeable, without significant stenosis.

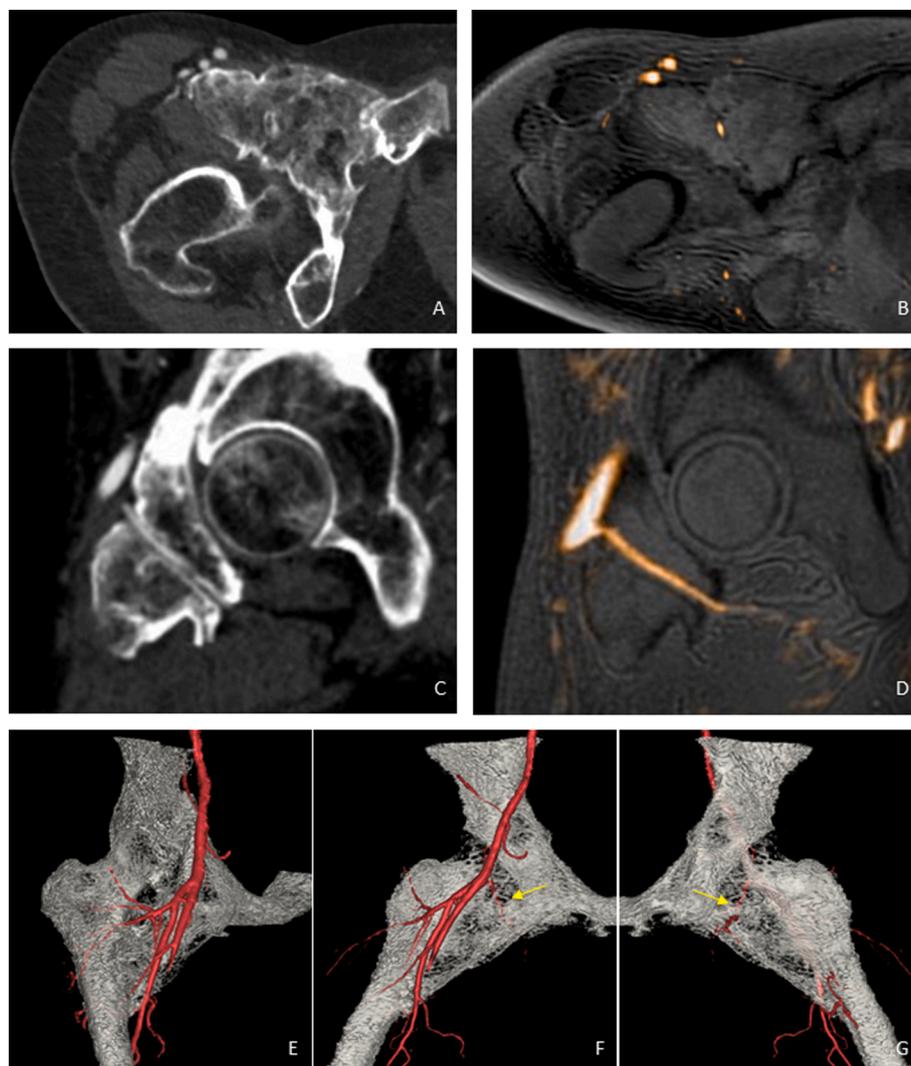


Fig. 4. Tunnel of the medial circumflex femoral artery in an anterior NHO of the right hip. Comparison of CTA and MRI (ZTE + MRA sequences) in axial (A and B) and sagittal (C and D) reconstructions. 3D Volumetric rendering on MRI in anterior (E), anterior-internal (F) and posterior (G) views.

Table 3

Relations of NHO to the vessels Five arteries analyzed for 30 NHO and 3 arteries for 1 NHO. Two veins analyzed for the 31 NHO.

Relation to arteries	
No involvement	91/153 (59 %)
Contact	24/153 (16 %)
Slight displacement	21/153 (14 %)
Gutter	8/153 (5 %)
Tunnel	9/153 (6 %)
Relation to veins	
No involvement	36/62 (58 %)
Contact	13/62 (21 %)
Slight displacement	12/62 (19 %)
Gutter	1/62 (2 %)
Tunnel	0/62 (0 %)

A contact was present in 15.7 % (n = 24/153), a slight displacement in 13.7 % (n = 21/153), a gutter in 5.2 % (n = 8/153) and a tunnel in 5.9 % (n = 9/153). Gutter and tunnel involved most often lateral and medial circumflex femoral arteries (Fig. 4).

Veins were distant from NHO in most patients. A contact or a slight displacement was present in 40.3 % (n = 25/62) and a gutter or a tunnel in 1.6 % (n = 1/62). There was one case of superficial and common

femoral venous thrombosis, that appeared in the interval between CT and MRI. Data are summarized in Table 3.

3.4. Relationships to nerves

Nerves were more often identified in MRI than in CT, respectively in 58 % (18/31) versus 39 % (12/31) for femoral nerve (Fig. 5) and 100 % (31/31) versus 97 % (30/31) for sciatic nerve. In anterior NHO, the femoral nerve was most often not identified. When identified, there was contact or slight displacement in 58 % (n = 7/12). Posterior NHO has most often contact with the sciatic nerve with a gutter or a tunnel in 56 % (n = 9/16) (Fig. 6). Data are resumed in Table 4.

In 14/31 hips, there was an important amyotrophy of gluteal muscles, quadriceps or adductor muscles, reported both on CT and MRI. Denervation edema was reported on MRI for 14 hips, independently of the amyotrophy, involving gluteal muscles in 10 hips, quadriceps muscles in 4 hips, adductor muscles in 4 hips and tensor fascia latae muscle in 4 hips (Fig. 1).

3.5. Agreement between CT and MRI assessments

Agreement between CT and MRI assessments were respectively very good (0.95, p < 0.001) for NHO location, very good (0.92, p < 0.001) for implantation, good (0.70, p < 0.001) for fragmentation and good (0.73,

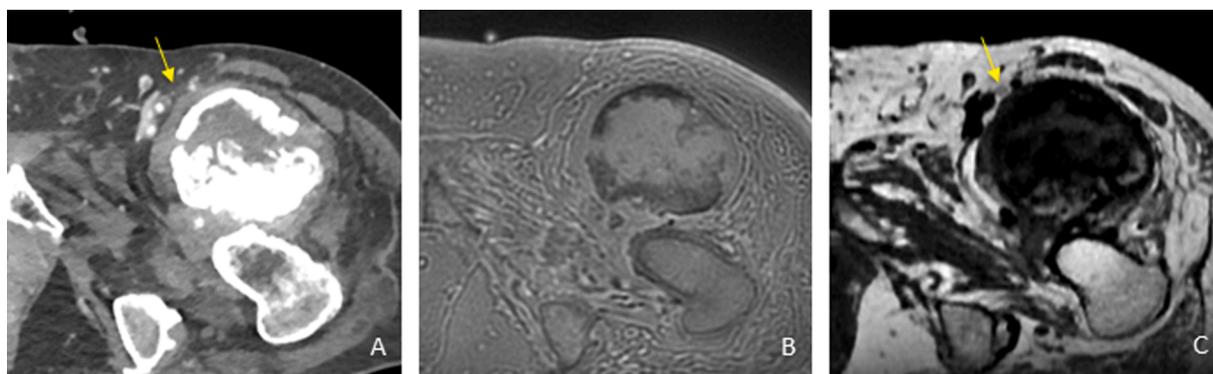


Fig. 5. Femoral nerve making contact in front of an anterior NHO of the left hip, at the lateral edge of the femoral artery. Axial images on CT-scan in soft tissues windows (A), on ZTE (B) and T1-weighted (C) sequences. Note that the femoral nerve (arrow) is almost not identified on CT while it is clearly identified on MRI.

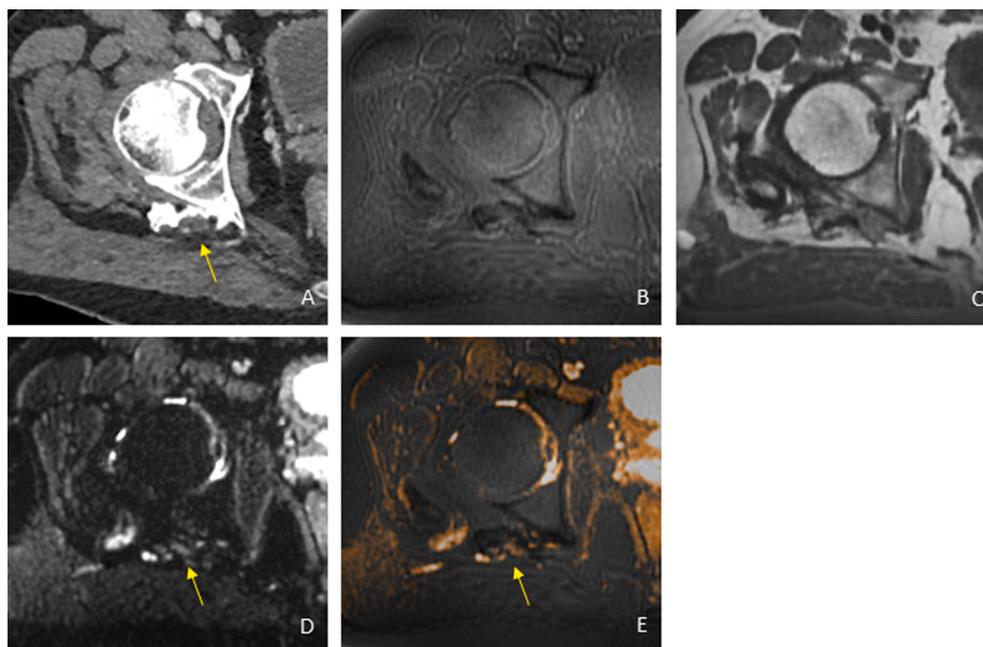


Fig. 6. Gutter of the sciatic nerve (arrow) in a posterior NHO of the right hip. Comparison of CT (A) and MRI on ZTE (B), T1-weighted (C) and STIR (D) sequences. Superposition of the ZTE and STIR sequences (E).

Table 4
Relations of NHO to the nerves.

Femoral nerve	
Visibility on CT	12/31
Visibility on MRI	18/31
No involvement	10/31 (32 %)
Contact	4/31 (13 %)
Slight displacement	3/31 (10 %)
Gutter	1/31 (3 %)
Tunnel	0/31 (0 %)
Non visualized	13/31 (42 %)
Sciatic nerve	
Visibility on CT	30/31
Visibility on MRI	31/31
No involvement	16/31 (52 %)
Contact	6 /31(19 %)
Slight displacement	0/31 (0 %)
Gutter	8/31 (26 %)
Tunnel	1/31 (3 %)

$p < 0.001$ for pseudarthrosis, good (0.66, $p < 0.001$) for contact with joint capsule, good (0.74, $p < 0.001$) for bone mineralization and very good (0.96, $p < 0.001$) for osteonecrosis.

There was a very good agreement for the relationship of NHO with the arteries (0.85, $p < 0.001$) and good agreement for the relationship with veins (0.76, $p < 0.001$).

Agreement for the relationship with the nerves was good (0.62, $p < 0.001$), respectively moderate (0.47, $p = 0.003$) for the femoral nerve and good (0.70, $p < 0.001$) for the sciatic nerve.

4. Discussion

This study demonstrated that MRI with dynamic MRA and ZTE sequences exhibited good or very good agreement with CT-scan for pre-surgical imaging of NHO, particularly for vascular analysis.

This is the first study to our knowledge to include MRA in the setting of pre-surgical assessment of NHO, associating ZTE sequence for osseous analysis and TRICKS sequence for vascular analysis. Moreover, MRI can better locate the nerves, particularly the femoral nerve for anterior NHO. MRI also evaluates denervation edema, as well as the trophicity of the muscles of the hip, which is very important for surgery and

rehabilitation.

However, analysis, post-processing and interpretation of MRI data require more time than for CT, in particular using ZTE sequences that are not frequently used in clinical practice.

Agreement between CT and MRI demonstrates that MRI provides excellent value on heterotopic ossifications and their relationships to vessels and nerves. This study may give insights into the use of MRI as an alternative to CT for pre-surgical assessment of NHO. MRI would be particularly useful in case of anterior NHO or if nerve involvement is suspected. Thus, MRI, even without TRICKS sequence, is an effective examination for patients with renal failure or iodine contrast media allergy. However, as a new technique, pre-surgical MRI assessment of NHO requires time and experience.

In this study, NHO presented approximately the same characteristics than in previous studies [9]. NHO location was anterior in 71 % versus 61 % and posterior in 52 % versus 52 %, with a little more often circumferential extension in 23 % versus 12 %. NHO were more often polyfragmented, in 81 % versus 63 %, and pseudarthrosis occurred in 65 % versus 42 %. Relationships to vessels were similar, since gutter and tunnel were reported in 5 % and 6 % versus 4,5% and 6 %. However, demineralization was more significant in this study. Mineralization was M1 or M2 in 56 % versus 79,5% and M3 or M4 in 44 % versus 20,5%. This may be explained because of a longer delay to surgery than a few years ago.

Surgery of NHO is complex and requires experimented surgeons. Indication depends on the limitation of joint amplitudes, on nerve compressions, or on the functional impact [3]. Unlike in oncologic surgery, the resection should not be exhaustive, to decrease potential morbidity. Only the part of NHO that limits joint amplitudes are removed and implantation bases should be respected to avoid the risk of iatrogenic fracture. The main intra-operative risk is hemorrhagic, mainly due to the relationships of NHO to vessels and intra-operative bleeding is frequent, then progressive hemostasis is carefully and progressively performed [7].

In addition, although surgery may be considered as the gold standard, it is not complete most of the time and all areas are not resected. Then, assessment of NHOs and their relationships to vessels and nerves is limited during surgery. This is why we considered the CT-scan as a gold-standard in this study.

However, CT is less accurate in assessing nerve involvement. As we reported in this study, nerves were more often identified in MRI than in CT-scan, particularly for the femoral nerve. The sciatic nerve is larger, and almost always identified in CT. This would indicate that it is better to perform MRI in case of anterior NHO.

The main limitation of this study is the small sample of patients included. Surgical indication of resection of NHO is limited and determined by a multidisciplinary team experienced in this pathology. Pre-surgical assessment was performed only in 31 hips (24 patients) from July 2019 to April 2022, with less than one patient per month. However, during the COVID-19 pandemic, surgery was not performed and only two patients were explored in 2020. Moreover, only one radiologist evaluated all CT and MRI. MRI interpretation requires radiologists with experience in pre-surgical NHO evaluation and experience in specific sequences such as ZTE or MRA. However, an inter-observer correlation should be interesting to attest the feasibility of MRI in daily practice.

Recently, NHO has been described as a possible complication for patients hospitalized due to severe COVID-19 infection [14,15]. Affected patients requiring surgical management will increase and MRI will probably be useful for optimal support.

In conclusion, MRI with dynamic MRA and ZTE sequences is a valuable alternative to CTA for pre-surgical assessment of NHO of the hip, in particular in anterior NHOs, if nerve involvement is suspected, or for patients with iodine contrast media allergy.

Informed consent

Written informed consent was obtained from all subjects (patients) in this study.

Ethical approval

Institutional review board approval was obtained.

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CRediT authorship contribution statement

Raphaël Amar: Writing – original draft, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision. **Marjorie Salga:** Investigation. **Mickaël Tordjman:** Writing – review & editing. **Nadia Venturelli:** Writing – review & editing. **Lionelle Nkam:** Formal analysis. **Madalina Jacota:** Methodology. **Lamiae Grimaldi-Bensouda:** Methodology. **Fabien Cale:** Investigation. **Robert-Yves Carlier:** Conceptualization, Supervision, Validation.

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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