

Clinical interest of quantitative bone SPECT-CT in the preoperative assessment of knee osteoarthritis

Romain De Laroche, MD^a, Erwan Simon, MD^b, Nicolas Suignard, MD^c, Thomas Williams, MD^c, Marc-Pierre Henry, MD^c, Philippe Robin, MD^{a,d,e}, Ronan Abgral, MD, PhD^{a,d,e}, David Bourhis, PD^{a,d,e}, Pierre-Yves Salaun, MD, PhD^{a,d,e}, Frédéric Dubrana, MD, PhD^{c,e}, Solène Querellou, MD^{a,d,e,*}

Abstract

The aim of the study was to evaluate the interest of quantitative bone SPECT-CT in the preoperative assessment of knee osteoarthritis (OA) before unicompartmental knee arthroplasty (UKA).

Patients eligible for UKA were prospectively included in 2 centers and underwent a preoperative SPECT-CT. Images were reconstructed with an OSEM, an OSCGM (allowing SUV quantification) and an enhanced OSCGM (containing uptakes to bones) algorithms. Visual analysis and quantification (SUVmax) were performed for each compartment (medial compartment [MC], lateral compartment [LC], and patellofemoral compartment [PFC]). Clinical data were preoperatively assessed. The gold standard was the per-operative OA staging (International Cartilage Repair Society [ICRS] scale). Spearman's correlation coefficient was used for correlations. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), and accuracy of SPECT-CT were assessed.

One hundred three patients (50 women, 53 men, mean age = 64.5 ± 10.3 y/o, 120 preoperative knees) were analyzed. There was no correlation between SUVmax and clinical data. There was a correlation between ICRS staging and SUVmax with both OSCGM (MC [$r_s = 0.25$], LC [$r_s = 0.51$], and PFC [$r_s = 0.27$]), and enhanced OSCGM, except in the PFC (MC [$r_s = 0.22$], LC [$r_s = 0.62$], and PFC [$r_s = 0.03$]). The Se, Sp, PPV, NPV, and accuracy of SPECT-CT were, respectively, 0.99, 0.67, 0.98, 0.80, 0.97 for the MC; 0.50, 0.85, 0.42, 0.89, 0.79 for the LC; and 0.23, 0.86, 0.50, 0.64, 0.62 for the PFC.

Bone SPECT-CT SUVmax is correlated with per-operative OA staging. Despite the low sensitivity of SPECT-CT in the LC, its high specificity in the LC should prompt the surgeon to be vigilant before UKA surgery.

Abbreviations: Acc = accuracy, ACL = anterior cruciate ligament, CT = computed tomography, FWHM = full width at half maximum, ICRS = International Cartilage Repair Society, KOOS = Knee Injury and Osteoarthritis Outcome Score, LC = lateral compartment, MC = medial compartment, MOAB = metabolic osteoarthritis burden, MOAV = metabolic osteoarthritis volume, MRI = magnetic resonance imaging, NPV = negative predictive value, OA = osteoarthritis, OSCGM = ordered subset conjugate gradient minimization, OSEM = ordered subset expectation maximization, PFC = patellofemoral compartment, PPV = positive predictive value, Se = sensitivity, Sp = specificity, SPECT = single photon emission computed tomography, SUV = standardized uptake value, TKA = total knee arthroplasty, UKA = unicompartmental knee arthroplasty, VRS = verbal rating scale.

Keywords: bone scintigraphy, knee arthroplasty, osteoarthritis, quantification, SPECT-CT, UKA

Editor: Michael Masoomi.

All authors disclose any financial and personal relationships with other people or organizations that could potentially and inappropriately influence (bias) their work and conclusions.

Clinical interest of quantitative bone SPECT-CT in the preoperative assessment of knee osteoarthritis.

The authors have no conflicts of interest to disclose.

^a Nuclear Medicine Department, University Hospital Morvan, Brest Cedex,

^b Orthopedic Surgery Department, Private Hospital of "La Baie", La vierge noire,

Morlaix, ^c Orthopedic Surgery Department, University Hospital Cavale Blanche,

Boulevard Tanguy Prigent, Brest Cedex, ^d EA 3878 GETBO IFR 148, Brest,

^e University of Bretagne Occidentale, France.

* Correspondence: Solène Querellou, Service de Médecine Nucléaire, Hopital MORVAN, 29200 Brest, France (e-mail: solene.querellou@chu-brest.fr).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Medicine (2018) 97:35(e11943)

Received: 16 March 2018 / Accepted: 26 July 2018

<http://dx.doi.org/10.1097/MD.00000000000011943>

1. Introduction

Knee osteoarthritis (OA) is one of the leading causes of global disability, with a worldwide age-standardized prevalence of 3.8%.^[1] Costs induced by this disease are important because of its high prevalence.^[2] Diagnosis remains based on clinical findings, and severity has to be assessed by imaging, particularly by plain radiography of the knee. Nonsurgical treatments are recommended in first intention for these patients.^[3] The primary goals of knee OA treatment are to relieve from pain with a high mobility joint. Refractory patients to these nonsurgical treatment options may be referred to joint surgery.^[4] Although high tibial osteotomy for treating or preventing knee OA is usually reserved to young patients with knee malalignment, the surgical treatment usually consists in total knee arthroplasty (TKA) or unicompartmental knee arthroplasty (UKA).

UKA quickly became an alternative treatment to TKA. The first unicompartmental knee prostheses were implanted in the 1970s.^[5] The idea was to replace only the osteoarthritic compartment, sparing the other ones. That is why OA has to be confined to a single compartment in patients undergoing an UKA procedure. Moreover, the anterior cruciate ligament (ACL) has to be functional.

It has been shown in many series that UKA improved outcomes of selected patients with unicompartmental knee OA.^[6,7] Advantages of UKA include shorter postoperative recovery, increased postsurgical ranges, and less perioperative morbidity (including thromboembolism, myocardial infarction, and stroke). Nevertheless, UKAs had worse implant survival both for revision and for revision/reoperation than TKAs at 8 years.^[7] Better accurate criteria for UKA indications appear to be fundamental to benefit from the advantages of UKA, without a too high revision or reoperation rate.

Criteria for UKA indications are still a matter of debate. Kozinn and Scott proposed in 1989 criteria based on clinical findings, including age, pain localization, body weight, ACL integrity, and knee deformity.^[8] Although these criteria are widely used, some of these contraindications seem obsolete. Indeed, surgery practice and prosthesis have changed since 1989. Some authors recently even proposed to ignore some of Kozinn's contraindications (such as chondrocalcinosis or patellofemoral OA),^[9] and to change some recommended thresholds (age, weight, activity) with good results.

Otherwise restriction of OA to a single compartment seems to be paramount to UKA success. Radiographic images may help in extent assessment, but it has been shown that there was a major discrepancy between radiographic and arthroscopic findings.^[10] Other imaging modalities, such as bone scintigraphy, have been assessed. Indeed, it has been used for many years as a marker of OA, due to its ability to predict joint space narrowing^[11] and after knee surgery.^[12] Moreover, volumetric scintigraphic imaging, single photon emission computed tomography (SPECT), combined with computed tomography (CT), appears to be a good tool to characterize knee OA^[13-16] and helps to select patients with unicompartmental knee OA.^[17]

Recent technological advances available in SPECT/CT, in particular new reconstructions, allow to quantify uptakes in bone SPECT-CT,^[18] with standardized uptake value (SUV) calculation as performed in PET/CT for oncological diseases. So we hypothesized that this tool could improve in the selection of patients before UKA, and we studied the potential interest of this quantitative tool in the preoperative assessment of UKA.

2. Method

2.1. Patients

Patients >18 years old eligible to UKA surgery for knee OA were prospectively included in 2 centers. Indication of UKA was assessed by an experienced orthopedic surgeon. Criteria of exclusion were contraindications for bone scintigraphy (pregnancy, breast feeding), signs of a multicompartmental knee OA indicating TKA surgery, such as diffuse and intense knee pain, or radiological severe multicompartmental knee OA, and consent refusal. All patients received oral and written information, and gave their oral and written consent. This study was approved by the ethics committee of our institution (NCT03145090).

2.2. Clinical data

All included patients underwent a bone scintigraphy in the nuclear medicine department of our institution. All patients had a clinical consultation with a nuclear medicine physician before radiopharmaceutical injection. Knee pain (according to a verbal rating scale [VRS] from 0 to 10) and location of the pain (medial,

lateral, anterior, posterior, diffuse, or other) were assessed by the physician. Moreover, a written dedicated knee OA score, the Knee injury and Osteoarthritis Outcome Score (KOOS), was completed by the patient. This score is divided into 5 parts: symptoms/stiffness, pain, function/daily living, function/sports/recreational activities, and quality of life. It is rated out of 100, 0 corresponding to an extremely painful and nonfunctional knee, 100 corresponding to a painless and totally functional knee.

2.3. Imaging

2.3.1. Image acquisition. Scintigraphic acquisitions consisted with an early planar acquisition (anterior and posterior views) of the knees 10 minutes after injection of 9 MBq/kg (0.24 mCi/kg) (500–800 MBq, 13.5–21.6 mCi) of ^{99m}Tc 3,3-diphosphono-1,2-propanedicarboxylic acid (DPD, Teceos, IBA Molecular, Gif-sur-Yvette, France) following by a whole-body acquisition completed by a SPECT-CT on a dual-headed gamma camera (Symbia Intevo T6, Siemens), centered on the knees, about 3 hours after injection. A low-energy high-resolution parallel-hole collimator was used for the acquisition. The energy window was set at 15%, centered on the photon energy peak of Tc-99m (140 keV). The SPECT acquisition protocol was as follows: 120 frames per detector head, each with duration of 10 seconds, acquired over 360° into a 256 × 256 matrix.

CT acquisition centered on the knees was performed immediately after the SPECT acquisition with a pitch of 1.0, tube voltage 130 kV, automatic mAs control (reference: 60 mAs), slice thickness 1.25 mm, matrix 512 × 512, field of view 30 cm. The CT reconstruction used a hard filter (B80s).

2.3.2. Image reconstruction. Scintigraphic data were reconstructed using 3 different algorithms:

1. The reference ordered subset expectation maximization (OSEM) 3D iterative algorithm (FLASH3D, Siemens) (OSEM-3D), 8 iterations, and 15 subsets with a 128 × 128 matrix (pixel size 4.8 × 4.8 × 4.8 mm), and a 12 mm full width at half maximum (FWHM) Gaussian postfilter.
2. The ordered subset conjugate gradient minimization (OSCGM) xSPECT algorithm (Siemens), allowing to perform SUV quantification thanks to the xSPECT Quant tool, 8 iterations and 6 subsets with a 256 × 256 matrix (pixel size 1.9 × 1.9 × 1.9 mm), and a 10 mm FWHM Gaussian postfilter.
3. The OSCGM-enhanced (OSCGM-e) xSPECTbone algorithm (Siemens), which uses CT data to constrain uptakes to bone structures, also allowing SUV quantification thanks to the xSPECT Quant tool, 8 iterations and 6 subsets with a 256 × 256 matrix (pixel size 1.9 × 1.9 × 1.9 mm), and a 10 mm FWHM Gaussian postfilter. Attenuation and scatter corrections were applied in the 3 reconstructions. Figure 1 shows an example of images obtained with the 3 reconstructions.

2.3.3. Image analysis. Images were interpreted by a nuclear medicine physician blinded from the clinical context. CT, SPECT, and fused SPECT-CT images were visualized with a commercially available interpretation software (Syngo.via, Siemens). To avoid memorization bias, each data set was interpreted with a 4 weeks interval.

Data set 1: Early planar images were interpreted according to a visual 3-point scale (0: no uptake; 1: moderate uptake; 2: intense uptake). Knee was divided into 2 parts: medial and lateral compartments. Only likely articular uptakes were taken into consideration; uptakes due to effusion were not.

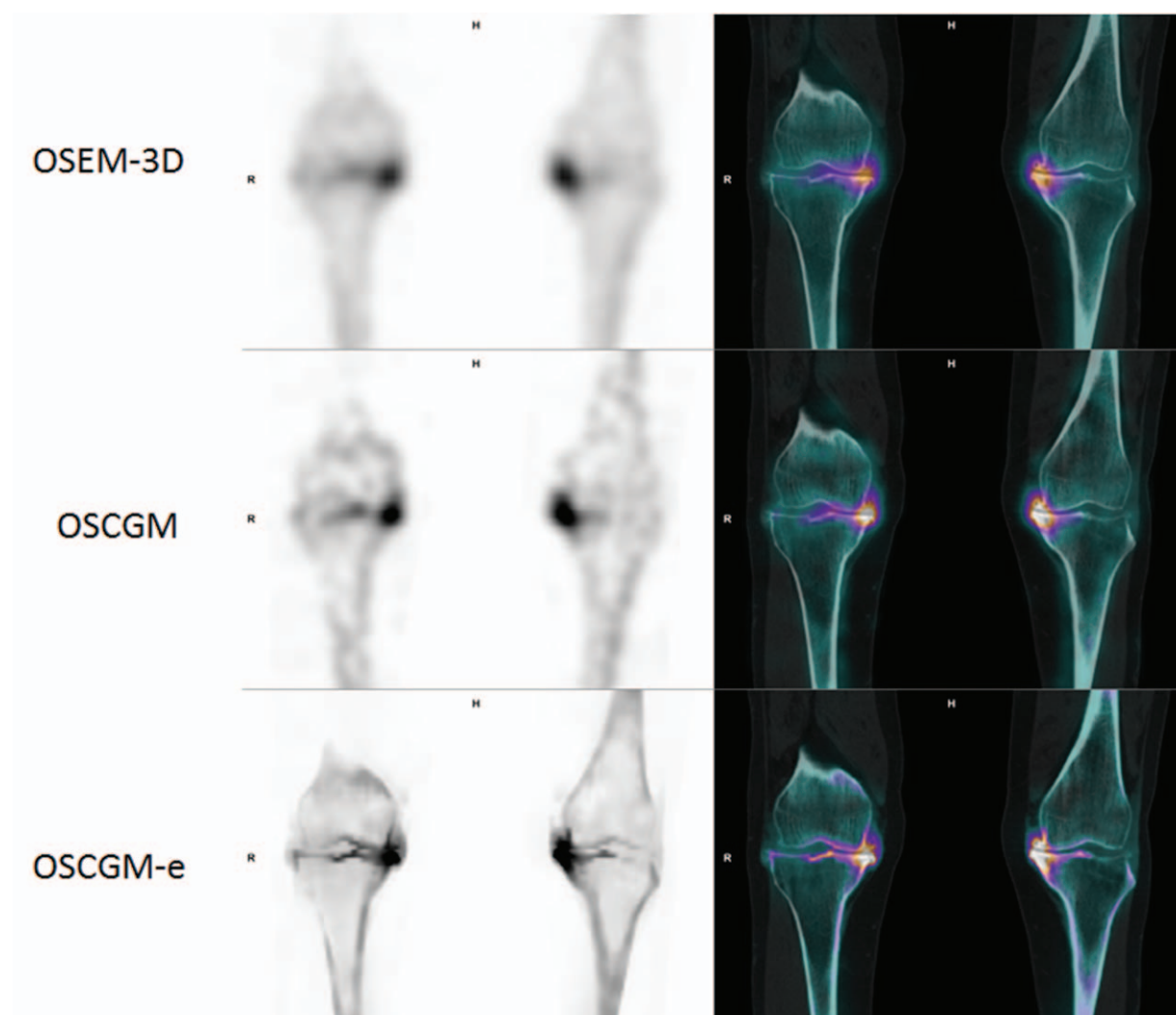


Figure 1. Example of SPECT and SPECT-CT images obtained with OSEM-3D, OSCGM, and OSCGM-e reconstructions (coronal views).

Data set 2: CT images of knee OA were assessed for each articular compartment (medial compartment [MC], lateral compartment [LC], and patellofemoral compartment [PFC]) according to a 3-point scale (0: no/minor OA; 1: moderate OA; 2: severe OA). CT signs of knee OA taken into consideration were joint space narrowing, sclerosis, osteophytes, and subchondral cysts.

Data set 3: OSEM-3D SPECT-CT images were visually assessed according to a 3-point scale (0: no uptake; 1: moderate uptake; 2: intense uptake, in comparison with the uptake of the cortical bone of the proximal tibial metaphysis) for the MC, LC, and PFC. CT images were available to localize the uptakes, but were not taken into consideration for the SPECT assessment. Uptakes of the tibial spines were not considered as MC, LC, nor PFC uptakes.

Data set 4: OSCGM SPECT-CT images were also visually assessed according to the same 3-point scale. SUVs measurements (SUVmax and SUVpeak) were performed to quantify the intensity of the uptake on each joint compartment visually considered as higher than the cortical bone of the ipsilateral proximal tibial metaphysis. SUVmax was the SUV value of the highest intensity voxel of the volume of interest (VOI). SUVpeak

was the maximum average SUV within a 1 cm^3 spherical volume, comprising the VOI.

Metabolic OA volume (MOAV), defined as the total volume of the voxels whose SUV was superior to 50% of the knee joint SUVmax, was also measured for the whole knee. Only joint uptakes voxels were included in the MOAV. Uptakes due to osteophytosis or enthesopathy were not included in the MOAV. Tibial spines uptakes were included into the MOAV. Metabolic OA burden (MOAB) was defined by the product of the MOAV and the SUVmean (SUVmean was the mean of the SUV values of the voxels included in the MOAV). Knee MOAB was calculated. MOAV and MOAB measurements were performed on MIM Software (v 6.6).

OSCGM-e SPECT-CT images benefited from the same per-compartment analysis, with visual and quantitative (SUVmax, SUVpeak, MOAV, and MOAB) measurements.

2.4. Per-operative assessment

Per-operative macroscopic findings of OA were considered as the gold standard. OA was assessed according to the International Cartilage Repair Society (ICRS) scale,^[19] which

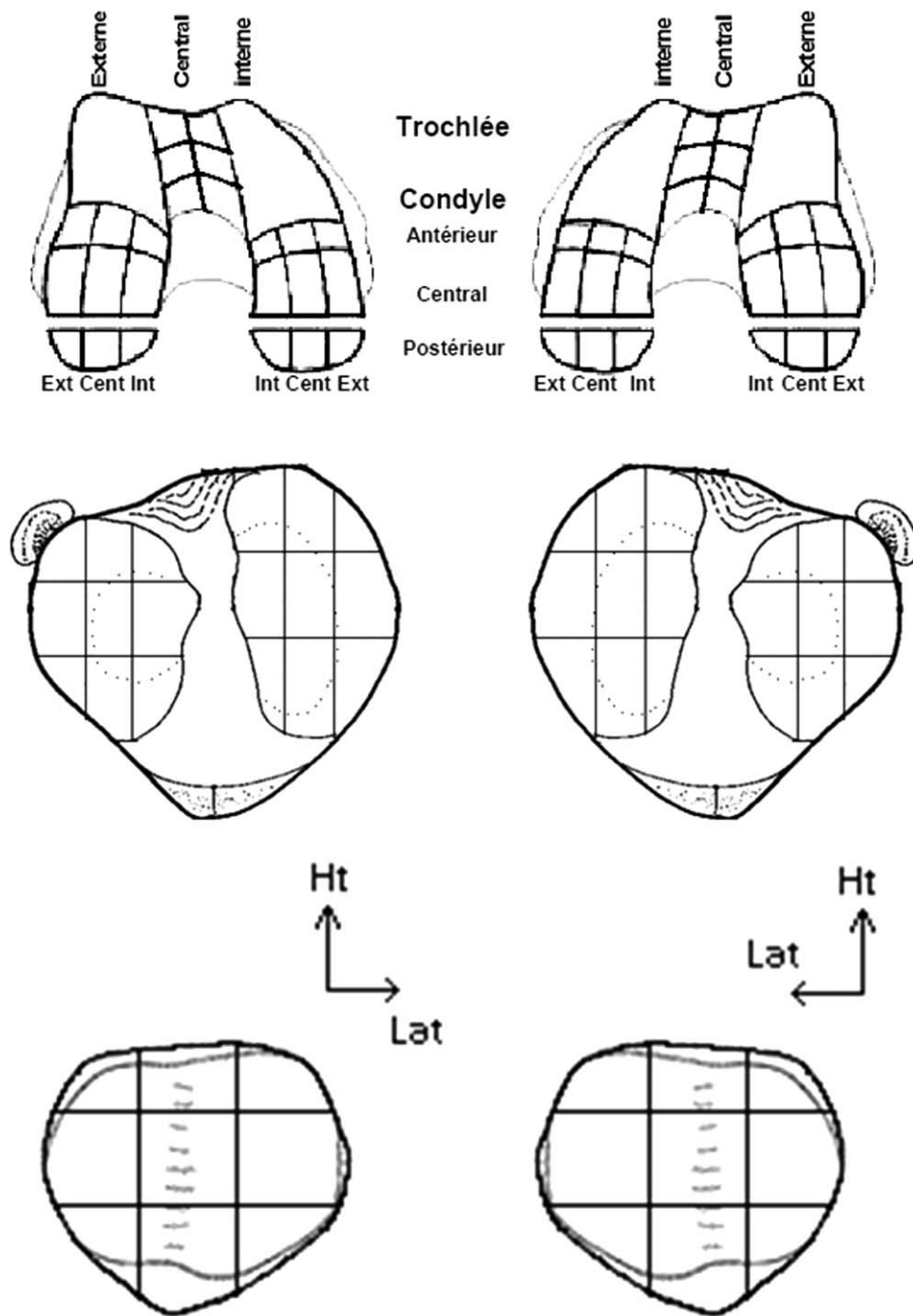


Figure 2. Form of per-operative findings.

rates OA from 0 (normal cartilage) to 4 (complete loss of cartilage thickness, bone only). Six articular surfaces were assessed: medial tibial plateau, lateral tibial plateau, medial femoral condyle, lateral femoral condyle, patella, and trochlea. Each of them was divided into 9 equal parts, with the exception of the trochlea, which was divided into 6. The orthopedic surgeon per-operatively assessed the OA ICRS stage for each part (Fig. 2). The maximum value of each compartment was considered as the OA stage of this compartment. For ethics condition, the orthopedic surgeon was aware of the scintigraphic findings.

2.5. Statistical analysis

Knees with planned surgery were analyzed. Spearman's correlation coefficient r_s was used for correlation analysis. A per-knee correlation was performed between clinical (KOOS, VRS) and imaging data (bone scintigraphy and CT). A per-compartment correlation was performed between per-operative ICRS staging and imaging (semi quantitative SPECT and CT) data. A value of $P < .05$ was considered as statistically significant.

The diagnostic performance of each SPECT-CT reconstruction and CT for knee OA in each compartment (sensitivity [Se], specificity [Sp], positive predictive value [PPV], negative predictive

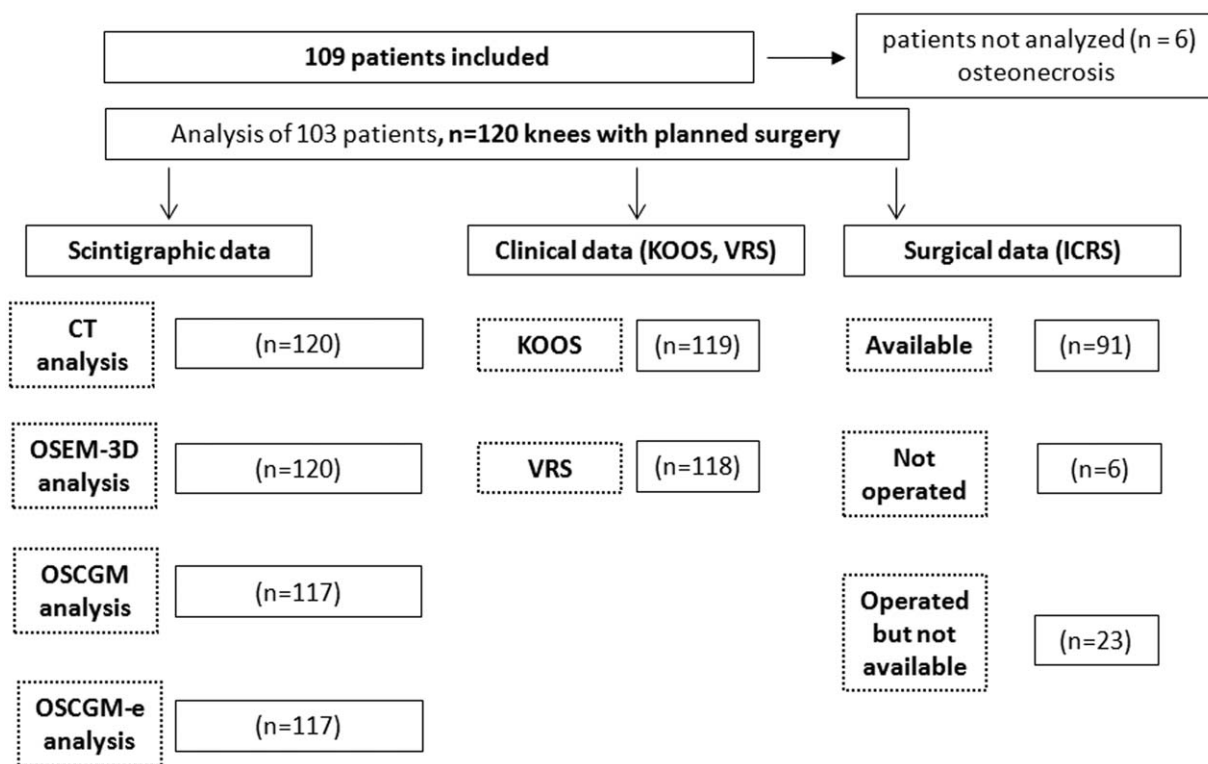


Figure 3. Flowchart of the study.

value [NPV], accuracy [Acc]) was assessed based on the visual analysis (1 or 2 were considered as positive, 0 as negative). A compartment was considered as positive according to the gold standard if its ICRS staging was 2 or higher.

3. Results

From March 2015 to July 2016, 109 patients were included. Six patients were excluded from the analysis because of per-operative finding of osteonecrosis of the medial or lateral femoral condyle. The flow chart of the study describes the data available (Fig. 3). One hundred three patients (50 women, 53 men, mean age = 64.5 ± 10.3 years), corresponding to 120 knees, were analyzed.

Population is described in Table 1. Ninety-one knees were included in the per-compartment analysis. Knee OA was per-operatively assessed (Table 2). Three joint surfaces could not be

evaluated by the surgeon (1 medial and 1 lateral tibial plateaus, and 1 trochlea). Mean delay between bone scan and surgery was 56 ± 63 days.

There was no significant correlation between clinical data (KOOS, VRS) and SPECT or CT data (Table 3). Table 4 sums up the correlations between SUVmax/SUVpeak and CT data with ICRS per-operative staging for MC, LC, and PFC for both OSCGM and OSCGM-e reconstructions. SUVmax and SUVpeak were correlated with ICRS staging (except PFC with OSCGM-e). CT was less correlated with ICRS staging than bone scintigraphy in the LC.

Considering ICRS stage 2 or over as significant OA, in OSEM-3D reconstruction, in the MC, Se was 0.99 [0.94; 1.00], Sp 0.67 [0.30; 0.90], PPV 0.98 [0.92; 0.99], and NPV 0.80 [0.38; 0.96]. In the LC, Se was 0.50 [0.28; 0.72], Sp 0.85 [0.76; 0.92], PPV 0.42 [0.23; 0.64], and NPV 0.89 [0.80; 0.94]. And in the PFC, Se was 0.23 [0.12; 0.39], Sp 0.86 [0.74; 0.93], PPV 0.50 [0.28; 0.72], and NPV 0.64 [0.53; 0.74]. Performance of bone SPECT-CT with the 3 reconstructions is detailed in Figure 4. Sensitivity of

Table 1
Characteristics of the 103 analyzed patients.

Sex	Women	50
	Men	53
Age	Mean ± SD	64.5 ± 10.3
	Range	35–84
Surgery planned	Unilateral UKA	86
	Bilateral UKA	17
Arthroplasties performed in the 91 knees included in the per-compartment analysis	Medial UKA	82
	Lateral UKA	8
	Medial+PF UKAs	1

PF=patellofemoral, SD=standard deviation, UKA=unicompartmental knee arthroplasty.

Table 2
Peroperative characteristics of knee osteoarthritis of the 91 operated knees included in the per-compartment analysis.

	MC	LC	PFC
ICRS 0	5	69	53
ICRS 1	1	6	3
ICRS 2	4	6	15
ICRS 3	18	2	17
ICRS 4	63	8	3

LC=lateral compartment, MC=medial compartment, PFC=patellofemoral compartment.

Table 3
Correlations (r_s) between whole knee scintigraphic/CT and clinical data.

		Knee VRS (0–10)	KOOS (100–0)
Early planar scintigraphic images	Early uptake images (0, 1, 2)	$r_s=0.02$	$r_s=-0.02$
Visual analysis (OSCGM, OSCGM-e, and OSEM-3D reconstructions)	VA knee OSEM-3D (0, 1, 2)	$r_s=0.09$	$r_s=-0.08$
	VA knee OSCGM (0, 1, 2)	$r_s=0.05$	$r_s=-0.13$
OSCGM quantitative parameter r_s	VA knee OSCGM-e (0, 1, 2)	$r_s=0.01$	$r_s=-0.11$
	Knee SUVmax OSCGM	$r_s=0.10$	$r_s=-0.11$
	Knee SUVpeak OSCGM	$r_s=0.10$	$r_s=-0.10$
	Knee MOAV OSCGM	$r_s=0.04$	$r_s=0.08$
OSCGM-e quantitative parameter r_s	Knee MOAB OSCGM	$r_s=0.11$	$r_s=-0.02$
	Knee SUVmax OSCGM-e	$r_s=0.08$	$r_s=-0.09$
	Knee SUVpeak OSCGM-e	$r_s=0.09$	$r_s=-0.09$
	Knee MOAV OSCGM-e	$r_s=0.05$	$r_s=0.04$
CT	Knee MOAB OSCGM-e	$r_s=0.12$	$r_s=-0.06$
	CT knee OA (0, 1, 2)	$r_s=0.09$	$r_s=0.02$

VA=visual analysis, VRS=visual rating scale.
No P value was inferior to .05.

bone SPECT (OSEM-3D) for ICRS III-IV knee OA was 1.0 [0.95; 1.0] for MC, 0.80 [0.49; 0.94] for LC, and 0.30 [0.15; 0.52] for PFC.

Performance of bone SPECT was depending on the type of planned UKA. In the 83 operated knees with medial UKA indication, performance of bone SPECT (according to OSEM-3D reconstruction with visual analysis) for the diagnosis of lateral OA (ICRS ≥ 2) was as follows: Se=0.00 [0.00; 0.32], Sp=0.85 [0.76; 0.92], PPV=0.00 [0.00; 0.26], NPV=0.89 [0.80; 0.94], and Acc=0.77 [0.67; 0.85]. Sixteen patients presented a lateral OA (ICRS ≥ 2). Eight of these patients had an ICRS 4 lateral OA. They were all planned for lateral UKA and were all detected by visual analysis according to the OSEM-3D reconstruction. The 8 other patients were all planned for medial UKA, and had an ICRS 2-3 lateral OA (6 patients with ICRS 2 and 2 patients with ICRS 3 OA). None of these 8 patients was detected by visual analysis according to OSEM-3D reconstruction.

4. Discussion

The preoperative assessment of knee OA is currently based on clinical and plain radiographic criteria. While it is established that clinical findings are not well correlated with plain radiographic,^[20] it has been shown that there was a major discrepancy between radiographic and macroscopic per-operative findings.^[10] Other imaging modalities have emerged to improve the diagnostic accuracy of knee OA. MRI is a good tool to assess location of knee OA^[21] and bone SPECT has been shown to be a good imaging modality in this indication,^[13] to select patients for UKA.^[17]

To the best of our knowledge, this is the first study assessing the correlation between quantitative bone SPECT and per-operative staging of knee OA. Kim et al have shown that SUVmax was

correlated with other imaging modalities, such as plain radiographs and MRI for the MC,^[22] but the correlation between OA per-operative staging and quantitative SPECT parameters has not been tested.

Concerning the correlation between clinical (KOOS and VRS) and imaging data, bone SPECT was not correlated with clinical data in knees with planned surgery. Our results were discordant with a previous article: Kim et al^[14] showed a correlation between clinical and scintigraphic visual findings but these authors analyzed both knees of the patients. In our study, there was no statistical correlation between SPECT (SUVmax, SUVpeak, MOAV, and MOAB) or CT data with clinical findings. This suggests that in patients needing surgery, bone metabolism is not the main cause of symptoms.

Method for delineation of metabolic volume in nuclear medicine is still a matter of debate. For the MOAV, we have chosen a threshold of 50% of the SUVmax. This method probably overestimates the MOAV of the miduptake OA, and as a consequence, overestimates the MOAB of these lesions. A fixed threshold of SUV may not be the good solution because of the great variation of the background intensity. This could be improved by SUV normalization to skeletal volume.^[23] In effect, as Tc-99m DPD uptake is mainly contained to skeleton, body weight normalized SUV is higher in patients with high body mass index. Other methods, such as a threshold considering a percentage of the SUVmean of a reference region of interest, should be considered, and may improve OA delineation. MOAV delineation could be performed on both OSCGM and OSCGM-e images. However for the OSCGM-e reconstruction, using CT data to contain uptakes in bone voxels, it was often necessary to manually remove voxels away from the joint from the MOAV, particularly in case of knee effusion. In effect, knee effusion

Table 4
Correlations between ICRS and imaging data (SUVmax, SUVpeak, CT).

		ICRS MC	ICRS LC	ICRS PFC
SUVmax	OSCGM	$r_s=0.25$ ($P=.02$)	$r_s=0.51$ ($P<.01$)	$r_s=0.27$ ($P=.01$)
	OSCGM-e	$r_s=0.22$ ($P=.04$)	$r_s=0.62$ ($P<.01$)	$r_s=0.03$ ($P=.74$)
SUVpeak	OSCGM	$r_s=0.25$ ($P=.02$)	$r_s=0.51$ ($P<.01$)	$r_s=0.27$ ($P=.01$)
	OSCGM-e	$r_s=0.23$ ($P=.03$)	$r_s=0.63$ ($P<.01$)	$r_s=0.04$ ($P=.71$)
CT		$r_s=0.26$ ($P=.01$)	$r_s=0.22$ ($P=.03$)	$r_s=0.30$ ($P<.01$)

LC=lateral compartment, MC=medial compartment, PFC=patellofemoral compartment.

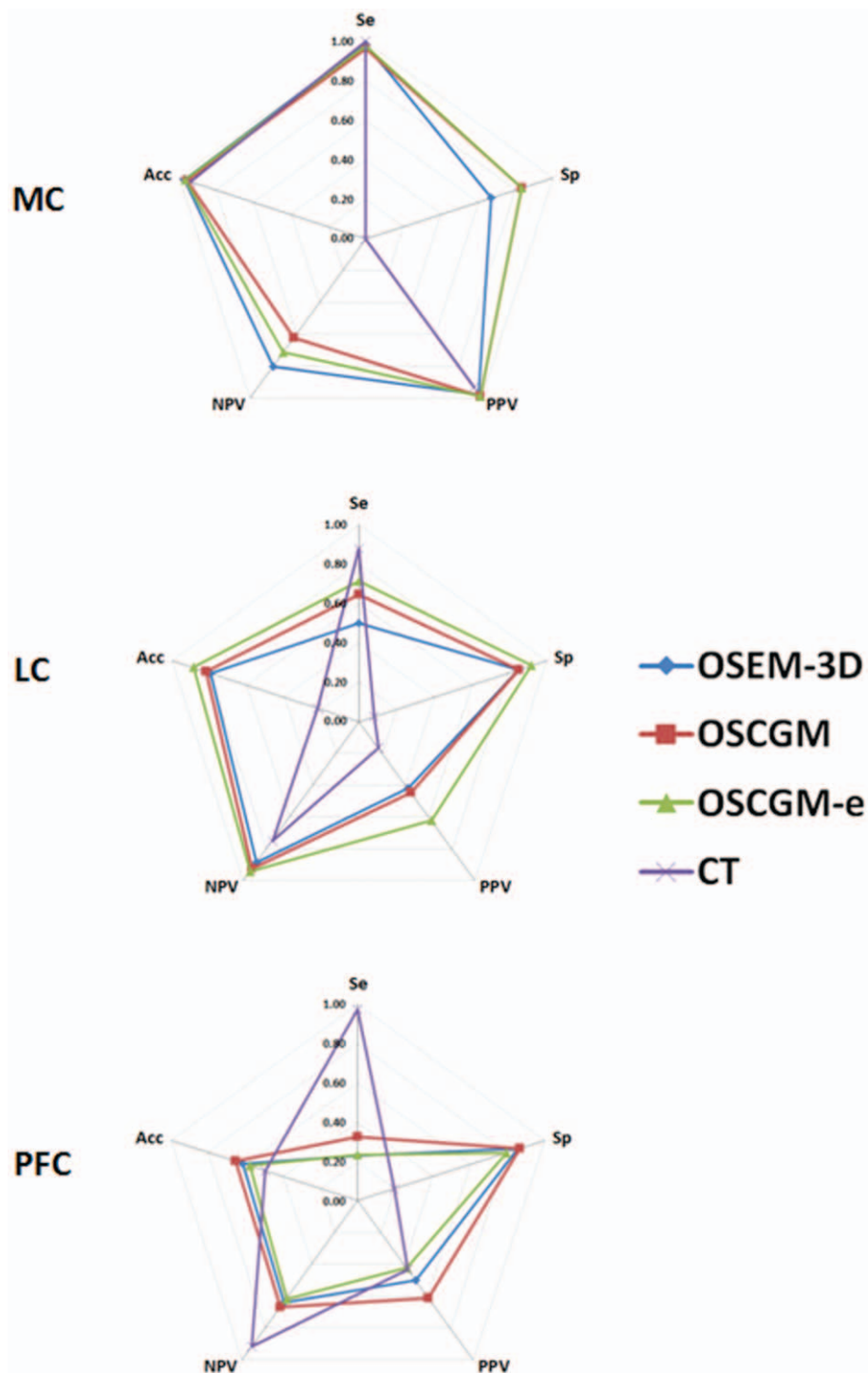


Figure 4. Performance of SPECT-CT and CT in the diagnosis of knee OA in the MC (upper graph), the LC (middle graph), and the PFC (lower graph).

uptake is commonly seen in DPD bone scan. As a consequence, on OSCGM-e images, we observed expanded cortical uptakes, that needed manual intervention, which may reduce the interobserver reproducibility of MOAV and MOAB.

We found in a significant cohort a statistically significant correlation between bone SPECT quantitative parameters and per-operative OA staging in the 3 knee compartments. Per-operative staging was correlated with both SUVmax and SUVpeak in the 3 knee compartments, except for the PFC in

the OSCGM-e images. This could be due to effusion uptakes, which are contained to bone in the OSCGM-e images, leading to artifactual bone uptakes. Medial and lateral compartment SUVmax could help to predict ICRS staging before surgery.

The performance of bone SPECT (OSEM-3D reconstruction) was excellent for the MC, considering the per-operative assessment of knee OA as a gold standard. Sensitivity was 0.99 [0.94; 1.00] and specificity was 0.67 [0.30; 0.90] (the 95% confidence interval of specificity was much wider because most

patients underwent UKA surgery for MC OA). This high sensitivity could be explained by the high proportion of ICRS 4 OA in the medial compartment (70%). Hart et al also found an excellent sensitivity for the detection of medial OA.^[17] In their study, medial OA were all grade 4 OA (according to the Outerbridge classification^[24]), in patients with indication of medial UKA. In the LC, considering the 83 knees with indication of medial UKA, sensitivity of bone SPECT (OSEM-3D reconstruction) in our study for the detection of ICRS 2 or more OA was 0.00 [0.00; 0.32]. This sensitivity is way insufficient, and does not allow the surgeon to dispense with per-operative exploration of the LC. It has already been shown that bone scan was not able to detect ICRS 1 and 2 OA in the LC.^[17] In our series, 8 patients with medial UKA indication had a LC OA of ICRS 2 or more. Out of these 8 patients, lateral OA (2 patients with grade 3, and 6 patients with grade 2) was not detected in the bone SPECT images in any patient. If we consider our whole series (91 analyzed knees), out of the 8 ICRS 4 lateral OA, all patient showed an intense uptake. These 8 detected lesions were in patients in which a lateral UKA was planned. If bone SPECT performance is excellent for grade 4 lateral knee OA, it looks insufficient for grade 2 and grade 3. Moreover, this suggests that bone scan is more a tracer of loading history of the compartments of the knee, like Hirschmann et al showed it,^[25] than OA. On the other side, specificity for the LC was 0.85 [0.76; 0.92] (OSEM 3D reconstruction). This good specificity should warn the surgeon about a potential indication of TKA (in case of planning a medial UKA) when the bone scan is positive in the LC.

Our results about the low sensitivity of bone SPECT for lateral OA in patients with indication of medial UKA run contrary to the current literature. In the series of Hart et al,^[17] 114 patients underwent a bone SPECT before knee arthroplasty. One hundred patients did not show lateral uptake: 73 had no lateral OA, 24 had grade 1 lateral OA, and 3 had grade 2 lateral OA (according to the Outerbridge classification^[24]). Fourteen patients showed lateral uptake: they all had grade 3 lateral OA. According to their data, the authors concluded that bone SPECT was a reliable tool to select patients for UKA. In another study by Jeer et al^[13] about 45 patients undergoing bone SPECT before medial UKA, 8 patients presented a lateral femoral condyle OA (mild OA for the 8 of them, according to the Jackson's classification^[26]). Six of these 8 lesions were detected on the bone scan. Six patients presented a lateral tibial plateau OA: only one of them was detected on the bone SPECT. The data of our study confirm the lack of sensitivity of bone SPECT in the LC before medial UKA surgery.

The performance of bone SPECT in the PFC was low. The sensitivity was 0.23 [0.12; 0.39] (OSEM-3D images). None of the 3 ICRS 4 patellofemoral OA was detected on the SPECT images. As a consequence, bone SPECT performance is insufficient to dispense with per-operative exploration. Like for the LC, specificity was good (0.86 [0.74; 0.93]), but assessment of patellofemoral OA seems to be of lower importance to select patients for UKA.^[9]

Our prospective study has some limits. First, there was only one reader, which does not allow to perform the inter-reader agreement of the bone SPECT-CT. Then, the CT acquisition performed was low-dosed. As a consequence, it may be hardly comparable with conventional CT scan performed for diagnosis of OA. Lastly, the per-operative data of 23 patients were not gathered, corresponding to 19% of the analyzed knees.

5. Conclusion

This original study challenges the reliability of bone SPECT-CT to select patients for UKA because of the lack of sensitivity in the LC in patients with medial UKA indication. In our series, bone SPECT was more specific but less sensitive than CT for the assessment of lateral and patellofemoral OA. The good specificity of bone SPECT in the LC should warn the surgeon about possible indication of TKA. Quantitative bone SPECT data (SUVmax, SUVpeak) are correlated with intraoperative assessment of OA according to the ICRS scale. The follow-up of this cohort will allow to assess if the uptake in the other compartment is predictive of UKA failure.

All authors disclose any financial and personal relationships with other people or organizations that could potentially and inappropriately influence (bias) their work and conclusions.

Author contributions

Conceptualization: Romain de Laroche, Erwan Simon, Nicolas Suignard, Thomas Williams, Marc-Pierre Henry, Philippe Robin, Ronan Abgral, David Bourhis, Pierre-Yves Salaun, Frédéric Dubrana, Solène Querellou.

Data curation: Romain de Laroche, Solène Querellou.

Formal analysis: Romain de Laroche, Solène Querellou.

Funding acquisition: Romain de Laroche.

Investigation: Erwan Simon, Nicolas Suignard, Thomas Williams, Marc-Pierre Henry, Frédéric Dubrana, Solène Querellou.

Methodology: Philippe Robin, Ronan Abgral, David Bourhis, Pierre-Yves Salaun, Solène Querellou.

Software: David Bourhis.

Supervision: Romain de Laroche, Pierre-Yves Salaun, Solène Querellou.

Visualization: Romain de Laroche.

Writing – original draft: Romain de Laroche.

Writing – review and editing: Romain de Laroche, Philippe Robin, Pierre-Yves Salaun, Solène Querellou.

References

- [1] Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis* 2014;73:1323–30.
- [2] Salmon JH, Rat AC, Sellam J, et al. Economic impact of lower-limb osteoarthritis worldwide: a systematic review of cost-of-illness studies. *Osteoarthritis Cartilage* 2016;24:1500–8.
- [3] McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage* 2014;22:363–88.
- [4] Osteoarthritis: care and management | 1-recommendations | Guidance and guidelines | NICE. [cité 21 févr 2017]. Available at: <https://www.nice.org.uk/guidance/cg177/chapter/1-recommendations?unlid=3944578782017215145321>.
- [5] Jamali AA, Scott RD, Rubash HE, et al. Unicompartamental knee arthroplasty: past, present, and future. *Am J Orthop Belle Mead NJ* 2009;38:17–23.
- [6] Hopper GP, Leach WJ. Participation in sporting activities following knee replacement: total versus unicompartamental. *Knee Surg Sports Traumatol Arthrosc Off J ESSKA* 2008;16:973–9.
- [7] Liddle AD, Judge A, Pandit H, et al. Adverse outcomes after total and unicompartamental knee replacement in 101,330 matched patients: a study of data from the National Joint Registry for England and Wales. *Lancet Lond Engl* 2014;384:1437–45.
- [8] Kozinn SC, Scott R. Unicompartmental knee arthroplasty. *J Bone Joint Surg Am* 1989;71:145–50.
- [9] Pandit H, Jenkins C, Gill HS, et al. Unnecessary contraindications for mobile-bearing unicompartamental knee replacement. *J Bone Joint Surg Br* 2011;93:622–8.

- [10] Fife RS, Brandt KD, Braunstein EM, et al. Relationship between arthroscopic evidence of cartilage damage and radiographic evidence of joint space narrowing in early osteoarthritis of the knee. *Arthritis Rheum* 1991;34:377–82.
- [11] Dieppe P, Cushnaghan J, Young P, et al. Prediction of the progression of joint space narrowing in osteoarthritis of the knee by bone scintigraphy. *Ann Rheum Dis* 1993;52:557–63.
- [12] Hirschmann MT, Amsler F, Rasch H. Clinical value of SPECT/CT in the painful total knee arthroplasty (TKA): a prospective study in a consecutive series of 100 TKA. *Eur J Nucl Med Mol Imaging* 2015;42:1869–82.
- [13] Jeer PJS, Mahr CC, Keene GCR, et al. Single photon emission computed tomography in planning unicompartmental knee arthroplasty. A prospective study examining the association between scan findings and intraoperative assessment of osteoarthritis. *Knee* 2006;13:19–25.
- [14] Kim H-R, So Y, Moon S-G, et al. Clinical value of (99m)Tc-methylene diphosphonate (MDP) bone single photon emission computed tomography (SPECT) in patients with knee osteoarthritis. *Osteoarthritis Cartilage* 2008;16:212–8.
- [15] Huellner MW, Strobel K. Clinical applications of SPECT/CT in imaging the extremities. *Eur J Nucl Med Mol Imaging* 2014;41(Suppl. 1):S50–8.
- [16] Vellala RP, Manjure S, Ryan PJ. Single photon emission computed tomography scanning in the diagnosis of knee pathology. *J Orthop Surg Hong Kong* 2004;12:87–90.
- [17] Hart R, Konvicka M, Filan P, et al. SPECT scan is a reliable tool for selection of patients undergoing unicompartmental knee arthroplasty. *Arch Orthop Trauma Surg* 2008;128:679–82.
- [18] Vija HA. Introduction to xSPECT technology: evolving multi-modal SPECT to become context-based and quantitative. *Siemens Med Solut USA* 2014.
- [19] Kleemann RU, Krockner D, Cedraro A, et al. Altered cartilage mechanics and histology in knee osteoarthritis: relation to clinical assessment (ICRS Grade). *Osteoarthritis Cartilage* 2005;13:958–63.
- [20] Claessens AA, Schouten JS, van den Ouweland FA, et al. Do clinical findings associate with radiographic osteoarthritis of the knee? *Ann Rheum Dis* 1990;49:771–4.
- [21] Raynauld J-P, Martel-Pelletier J, Berthiaume M-J, et al. Quantitative magnetic resonance imaging evaluation of knee osteoarthritis progression over two years and correlation with clinical symptoms and radiologic changes. *Arthritis Rheum* 2004;50:476–87.
- [22] Kim J, Lee H-H, Kang Y, et al. Maximum standardised uptake value of quantitative bone SPECT/CT in patients with medial compartment osteoarthritis of the knee. *Clin Radiol* 2017;72:580–9.
- [23] Carvalho G, Marin JFG, Garcez AT, et al. SUV normalized by skeletal volume on 18F-fluoride PET/CT studies. *Clin Nucl Med* 2016;41:529–33.
- [24] Outerbridge RE. The etiology of chondromalacia patellae. 1961. *Clin Orthop* 2001;389:5–8.
- [25] Hirschmann MT, Schön S, Afifi FK, et al. Assessment of loading history of compartments in the knee using bone SPECT/CT: a study combining alignment and 99mTc-HDP tracer uptake/distribution patterns. *J Orthop Res Off Publ Orthop Res Soc* 2013;31:268–74.
- [26] Jackson RW. Arthroscopic surgery and a new classification system. *Am J Knee Surg* 1998;11:51–4.