A Three-dimensional Method for Evaluating Changes in Acetabular Osteolytic Lesions in Response to Treatment

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Abstract The treatment of asymptomatic osteolysis among well-fixed cementless cups remains controversial. To compare the effectiveness of different treatment strategies, an objective technique for evaluating bone remodeling would be useful. By matching and comparing serial CT images with the aid of a computer-assisted imaging program, we developed a method to evaluate three-dimensional mineralization changes within osteolytic defects. Preoperative, immediate postoperative, and followup CT images were normalized based on a phantom with known densities and matched using image registration so that the same region could be analyzed on each image. New bone mineralization within the preoperative osteolytic lesion volume was quantified based on a patient-specific trabecular bone density threshold. As a pilot study, we applied this technique in 10 patients treated by polyethylene liner exchange with débridement and grafting of periacetabular osteolytic lesions using a calcium sulfate bone graft substitute. Relative to the preoperative

osteolytic lesion volume, an average of 43% (range, 8%–72%) of each defect was filled with graft at revision. After resorption of the graft, an average of 24% (range, 9%–44%) of the original defect volume demonstrated evidence of new mineralization at 1-year followup. The amount of new mineralization was directly proportional ($r^2 = 0.70$) to the defect filling achieved at revision. CT-based image analysis offers an objective method for quantifying three-dimensional bone remodeling and can be used to evaluate the effectiveness of osteolysis treatment strategies.

Level of Evidence: Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Although asymptomatic osteolysis associated with well-fixed cementless cups is a relatively common finding at late followup, management of this condition remains controversial [7, 24, 29, 33]. Some surgeons have advocated delayed intervention, observing the patients are typically asymptomatic, surgical treatment can lead to complications, and the incidence of late loosening or pelvic fracture associated with osteolysis appears to be low [2, 4, 6, 9, 11, 14, 15]. Others have recommended surgery with the goal of arresting the bone loss and avoiding cup loosening [5, 16, 27, 30, 34]. Current surgical options include polyethylene liner exchange or complete cup revision, both of which can be performed with or without débridement and bone grafting of the osteolytic defects [1, 13, 23, 26, 35]. When bone grafting has been employed, investigators have typically reported evidence of graft consolidation based on plain radiographs [17, 25, 35]. However, three-dimensional changes in bone, particularly of trabecular bone, cannot be

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accurately quantified due to the two-dimensional nature of plain radiographs.

Because of donor site morbidity associated with autogenous bone grafting and the risk of disease transmission associated with allograft, there has been sustained interest in developing alternative materials to fill osseous defects. At the current time, a variety of allograft-derived and synthetic bone graft substitutes are available that can be used in conjunction with other substances, such as bone morphogenic proteins, to treat osteolytic lesions [33]. Ideally, an analytic technique to quantify the three-dimensional bone remodeling of an osteolytic lesion would facilitate objective comparisons of clinical performance among different surgical techniques and graft materials such as injectable calcium sulfate-based bone graft substitutes [17, 31].

We therefore developed a method to quantify the three-dimensional bone remodeling using serial CT images. We then used the method in a small pilot series to illustrate how one might (1) identify and determine the volume of osteolytic lesions; (2) determine the amount of graft filling; and (3) determine whether the amount of defect filling achieved at the time of revision would correlate with the extent of new mineralization observed at followup.

Patients and Methods

To quantify three-dimensional mineralization within osteolytic lesions, we developed a technique that analyzes

serial CT scans using a commercially available computer-aided image analysis program (Analyze 7.0; AnalyzeDirect Inc, Overland Park, KS). CT scans were obtained as part of routine care during preoperative and postoperative followup. Multidetector machines (GE LightSpeedTM VCT; GE Healthcare, Milwaukee, WI; SomatomTM Sensation; Siemens, Munich, Germany) were used to perform helical scans at 140 kV. Each patient was imaged while supine from the anterosuperior iliac spine to the lesser trochanter with a phantom (Model 3 CT Calibration Phantom; Mindways Software Inc, Austin, TX) positioned beneath their pelvis. The phantom, incorporating five cylindrical rods with known water-equivalent and K₂HPO₄-equivalent densities, was used to calibrate and normalize each CT image. Using the raw CT scan data, a reconstruction of the entire pelvis with the phantom was obtained for calibration purposes (Fig. 1) and a higher-resolution image of the hip limited to a nominal 22-cm field of view was used for analysis purposes. Each CT image slice consisted of a 512 by 512 array of elements, commonly called pixels. Coupled with the slice thickness, the pixels created volume elements called voxels. Each voxel was associated with a Hounsfield number, ranging from −1024 to 3071, proportional to the density of the element. DICOM-formatted CT images were reconstructed in thin slices (1.0–1.25 mm) and transferred to a personal computer (Dell, Inc, Round Rock, TX) for analysis using the Analyze software.

A CT co-registration measurement technique was developed to objectively quantify changes between two CT

Fig. 1A–C A calibration phantom having five cylindrical rods with known densities was included with each CT scan. **(A)** An axial CT slice illustrates the rods with known densities embedded within the phantom at the bottom of the image. **(B)** The individual rods were segmented on each slice using image analysis software. **(C)** A three-dimensional reconstruction illustrates the relationship of the patient's pelvis to the calibration phantom. Each rod has a different density.

images at different time intervals. The volume of the osteolytic defect filled with bone graft substitute at the time of revision was determined by comparing an immediate postoperative CT with the preoperative CT. The volume of new mineralization at a later followup interval was determined by comparing a followup CT with the preoperative CT. The co-registration measurement technique consists of four steps.

The first step in our image analysis technique involved calibration and normalization of each CT image. After loading the CT image with the whole pelvis including the phantom, an analyst (HH) differentiated the cylindrical rods imbedded in the phantom from the rest of the image using a process known as segmentation (Fig. 1). After identifying the image volume associated with each rod, the average Hounsfield value was determined. A linear regression was performed using the average Hounsfield measurement from each of the five rods to determine the relationship between Hounsfield units and density. The regression results for each CT scan were used to transform the Hounsfield units associated with each voxel to an equivalent density value for the whole pelvic and single hip CT images obtained at each time point.

Although 140 kV was used to minimize image artifacts associated with high attenuation metal objects, the residual artifact in each slice varied depending on the amount and type of metal within the slice [38]. To examine the influence of artifacts on our analysis technique, each CT image was divided into two discrete regions calibrated separately. These regions consisted of the CT slices superior to the cup free of metal artifacts and the slices below the superior aspect of the cup that tended to have artifacts owing to the presence of the titanium alloy cup and cobalt-chromium alloy stem used at our institution.

The second step of the analysis involved matching a postoperative CT image with the preoperative CT from the same patient using a process known as registration. The CT registration was accomplished employing a normalized, mutual information-based voxel matching algorithm available in the Analyze software application. By using the artifact-free portions of the pelvis above the cup in CT images obtained at different times, the spatial orientation of the followup image was positioned to match the preoperative CT image. The initial positioning of the followup CT was specified by the operator and the software iteratively refined the position to optimize the matching between the CT images. The final result of the registration process was a transformation matrix that specified the three-dimensional translations and rotations that would effectively superimpose the pelvis from the patient's followup CT on the preoperative image.

The third step in the analysis involved defining specific regions of interest for evaluation of bone remodeling

within each CT image via a process called segmentation. Using the unilateral, preoperative CT image of the hip replacement, the boundaries of the osteolytic lesions were manually traced on each slice by a single, experienced reviewer (CH) to determine the volume and location of each osteolytic lesion [8, 19, 22, 32]. In addition, a cylinder with a volume of approximately 0.5 cm³ was manually defined within the iliac trabecular bone near the sacroiliac joint. Since this region was superior to the cup, the CT slices including the cylinder were free of metal artifacts. The distribution of voxel densities within the cylindrical volume was measured with the Analyze software to determine the mean and standard deviation. For the purposes of classifying a particular voxel within the CT image as bone, we established a trabecular bone threshold, which was defined as the mean density of the voxels within the cylindrical volume plus one standard deviation. Using this method, the density threshold used to define bone was based on each patient's specific trabecular bone density at a particular point in time.

The final analysis step involved automatically calculating the volume of material within the preoperative osteolytic lesion volume on each CT image having a density equal to or greater than the trabecular bone threshold. Before the CT images were evaluated, the data were conditioned by eliminating voxels with Hounsfield units representative of metal, bowel gas, air, or severe image artifact. This was accomplished by creating a mask that would retain only those voxels with a Hounsfield number between -500 and 1800 that coexisted in all serial CT images. After conditioning, each image was calibrated using the results from Step 1 and the followup CTs were transformed and interpolated to match the orientation of pelvis and the voxel locations in the preoperative CT using the results from Step 2. The volume of bone within the manually defined osteolytic lesion on the preoperative CT was evaluated by summing the voxels having a density equal to or greater than the trabecular bone threshold. Because the calcium sulfate was denser than trabecular bone, the amount of bone graft filling achieved at the time of revision was defined as the total volume of all voxels within the osteolytic lesion on the immediate postoperative CT with a density equal to or greater than the trabecular bone threshold minus the bone volume measured on the preoperative CT. Because the calcium sulfate radiographically disappeared by 4-month followup, new mineralization at subsequent followup intervals was defined as any voxel within the original preoperative osteolytic lesion volume having a density equal to or greater than the trabecular bone threshold on the followup CT minus the amount of preexisting bone measured on the preoperative CT.

As a pilot study, we applied our analysis technique to 10 patients who underwent a modular polyethylene liner

exchange and bone grafting of periacetabular osteolytic lesion using a calcium sulfate-based bone graft substitute (MIIG[®] X3 HiVisc; Wright Medical Technology, Inc, Memphis, TN). The patients consisted of seven men and three women (Table 1). The mean age at the time of revision was 56.3 years (range, 47.7–72.5 years). The original diagnosis was osteoarthritis in seven, developmental dysplasia in two, and posttraumatic osteoarthritis in one patient. The index revision was the first revision for all cases. The mean time from the primary THA to revision was 9.7 years (range, 5.8–16.4 years). The minimum followup post revision was 0.8 years (mean, 1.0 year; range, 0.8–1.4 years). All patients had prerevision radiographs demonstrating bone ingrown porous-coated femoral stems and stable porous-coated acetabular cups. All components were modular, allowing both head and liner exchange. The modular acetabular cups included nine Duraloc[®] (DePuy Orthopaedics, Inc, Warsaw, IN) and one ACS Triloc+ cup (DePuy). Medical information from these cases was reviewed retrospectively as part of an IRB-approved study.

The indication for surgery for these patients was impending wear-through of the polyethylene liner or rapidly progressive osteolysis. Impending wear-through was defined as less than 2 mm of residual liner thickness based on radiographic evaluation while rapidly progressive osteolysis was a more subjective assessment that depended on the age of the patient and the surgeon's experience. In nine cases, the same surgical approach was used for the primary and revision procedures, which included two lateral and seven posterolateral. One case used the same incision but an anterior approach for the primary and a posterolateral approach for the revision procedure. This patient had a greater trochanter fracture associated with osteolysis and the posterior revision approach was used to spare the anterior third of the gluteus medius, which

remained attached to the femur. At surgery, the polyethylene liner was exchanged for all THAs, but the metal cup was retained and osteolytic lesions were débrided to the best of the surgeon's ability using a malleable, stiff-bristled test-tube brush and other instruments available from the MIIG[®] HV Procedure Kit (Wright Medical) as previously described [12]. Defects were further débrided with pulsatile lavage after curetting and brushing. Rim lesions were typically curetted under direct visualization and finger-packed or the graft material was injected while sealing the defect by hand. Lesions behind the cup were accessed through holes in the cup or via a small bone window created during surgery, which could be used for calcium sulfate injection. Contained lesions communicating only with the central hole were injected under pressure with the calcium sulfate paste. We routinely attempted to maximize the amount of the lesion filled.

The components of the MIIG[®] bone graft material were packaged separately as a powder and a liquid, which were mixed at the time of surgery. Initially, the graft material could be injected as a high-viscosity liquid. Over several minutes, the material hardened to a puttylike consistency, which could be finger-packed. The calcium sulfate-based MIIG[®] material was chosen because of its handling characteristics, safety, osteoconductive properties, the availability of sufficient volumes to fill large defects, its radiographic visibility, and its ability to flow during filling with subsequent hardening that afforded the potential to provide temporary structural support and seal the communication pathways between the osteolytic lesion and the joint space while ensuring the graft material remained fixed until it resorbed [3, 10, 17, 18, 28].

Pearson's correlation was used to evaluate the relationship between osteolytic defect filling on the immediate postoperative CT image and new mineralization based on

Table 1. Patient demographics and clinical characteristics

Patient	Diagnosis	Gender	Age (years)	Primary to revision (years)	Revision to first followup (years)
1	Osteoarthritis	Male	50.8	5.8	0.8
2	Osteoarthritis	Male	56.2	11.2	1.0
3	Osteoarthritis	Male	53.4	8.3	1.0
4	Trauma	Male	72.5	16.4	1.0
5	Developmental dysplasia of the hip	Female	48.8	7.2	1.4
6	Osteoarthritis	Male	48.2	8.5	1.2
7	Osteoarthritis	Male	64.5	9.6	1.0
8	Developmental dysplasia of the hip	Female	47.7	9	1.0
9	Osteoarthritis	Male	63.2	9	1.1
10	Osteoarthritis	Female	57.9	11.6	1.0
Minimum			47.7	5.8	0.8
Maximum			72.5	16.4	1.4
Average			56.3	9.7	1.0

the followup CT image. All statistical analyses were performed using SPSS® (SPSS Inc, Chicago, IL).

Results

Among the 10 hips, we identified 20 discrete periacetabular osteolytic lesions on the preoperative CT scan (Table 2). The mean osteolytic lesion volume was 13.8 cm³ (range, 0.5–53.9 cm³). Three hips had a single osteolytic lesion, four hips had two osteolytic lesions, and three hips had three osteolytic lesions. Four lesions communicated with the rim, nine communicated with the single apical dome hole, six communicated with the rim and dome hole, and one lesion originated from a screw hole in the cup. Sixteen of 20 lesions were treated by débridement and grafting. The mean size of the 16 treated lesions was 16.8 cm³ (range, 1.4–53.9 cm³). The remaining four lesions were not treated at the time of surgery because of their relatively small size and the difficulty associated with accessing them. All untreated

lesions were located at the anterior rim and were not accessible through a lateral or posterolateral surgical approach.

On the postoperative CT, the graft material was clearly visible for all 16 treated lesions, even in the presence of image artifacts. Among all 16 treated defects, the mean percentage of lesion filling was 43% (range, 8%–72%). In one case, 4.8 cm³ of the graft material had extruded from the defect into the muscle belly of the gluteus medius due to cortical perforation of the ilium associated with the osteolytic defect. In all cases, evaluation of postoperative radiographs at nominal 4-month followup indicated complete resorption with no evidence of residual calcium sulfate graft material (Fig. 2).

At a minimum followup of 0.8 years (mean, 1.0 year; range, 0.8–1.4 years), 24% (range, 9%–44%) of the original osteolytic defect volume, on average, demonstrated evidence of new mineralization. Although there was some variation, new mineralization within the grafted lesions tended to be most pronounced in regions adjacent to where the boundaries of the graft material were observed on the

Table 2. Characteristics and treatment of osteolytic lesions

Patient	Lesion	Lesion type	Fill method	Lesion volume (cm ³)	Total		Artifact-free region		Metal artifact region	
					Fill at surgery	New mineral at followup	Fill at surgery	New mineral at followup	Fill at surgery	New mineral at followup
1	1	Dome	Injection	30.8	17%	22%	4%	14%	51%	44%
	2	Dome	Injection	1.4	9%	21%			9%	21%
	3	Rim	Not treated	1.3	–16%	14%			–16%	14%
2	4	Rim	Not treated	0.5	1%	0%	0%	0%	3%	0%
	5	Dome + rim	Injection	25.2	59%	35%	91%	72%	56%	32%
	6	Rim	Not treated	3	–24%	19%			–24%	19%
3	7	Dome	Injection	14.8	34%	23%	28%	20%	51%	32%
	8	Dome + rim	Injection	13.8	8%	24%			8%	24%
	9	Dome + rim	Injection	18.2	15%	9%	–2%	0%	15%	9%
4	10	Dome	Injection	43.5	66%	28%	69%	38%	64%	19%
	11	Rim	Not treated	2.2	4%	1%	1%	1%	38%	9%
5	12	Dome	Injection	3.3	58%	21%	65%	23%	7%	2%
	13	Dome + rim	Injection	6.9	38%	11%	6%	8%	50%	12%
6	14	Dome + rim	Injection	4.1	62%	26%	81%	46%	58%	22%
	15	Dome	Injection	8.5	61%	40%			61%	40%
7	16	Dome	Injection	53.9	47%	10%	70%	25%	40%	5%
8	17	Dome	Injection	1.8	28%	24%	38%	30%	–23%	–5%
	18	Dome + rim	Injection	15.8	71%	44%	27%	33%	71%	44%
9	19	Screw hole	Injection	6.4	37%	19%	44%	22%	–10%	3%
10	20	Dome	Injection	21.3	72%	31%	86%	29%	61%	24%
Treated lesions										
Minimum				1.4	8%	9%	–2%	0%	–23%	–5%
Maximum				53.9	72%	44%	91%	72%	71%	44%
Average				16.8	43%	24%	47%	28%	36%	20%

Fig. 2A–D A series of radiographs from a patient (Patient 7, Lesion 16; Table 2) treated for osteolysis by débridement and grafting illustrates evaluating acetabular bone remodeling is difficult on plain radiographs. (A) Although the lesion margins are not well demarcated on the prerevision radiograph, a preoperative osteolytic defect with a volume of 53.9 cm^3 was identified behind the dome hole on CT. (B) At revision, the lesion was grafted with MIIG[®] bone graft substitute

and analysis of the immediate postoperative CT indicated 47% of the original defect volume was filled with graft material. (C) By the 4-month followup, the graft material demonstrated complete resorption on radiographs. (D) Although the remodeling is ambiguous on radiographs, 10% of the original defect volume demonstrated evidence of new mineralization at 1-year followup on CT.

Fig. 3A–F A series of registered CT slices from Patient 4 (Table 2) demonstrates how our technique evaluates osteolytic lesion filling and bone remodeling. (A) The preoperative slice includes portions of two osteolytic defects defined by the yellow regions in (B). (C) A slice from the immediate postoperative CT demonstrates filling of the defect with MIIG[®] bone graft substitute, along with some extruded graft material in the periacetabular soft tissue. (D) The lesion filling is

identified as the red region and the original defect area as the yellow region. (E) At 1-year followup, the extruded graft material has completely resorbed and new mineralization appears most prominently along the margins of the original defect. (F) New mineralization is identified as the red region and the original defect area as the yellow region.

immediate postoperative CT (Figs. 3, 4). In contrast, untreated osteolytic defects had almost no new bone formation, but they also demonstrated no enlargement of the preoperative lesion volume (Fig. 5). In the one case where the graft material extruded outside the pelvis, it completely resorbed without any residual ossification of the soft tissue (Fig. 3). However, cortical hypertrophy was

noted on the exterior surface of the pelvis adjacent to where the calcium sulfate graft had extruded outside the bone (Fig. 3). On average, the percentage of the original defect volume demonstrating evidence of new mineralization was approximately 1/2 the percentage of the defect volume filled at the time of revision. Although metal-induced artifacts tended to introduce noise, analysis of the filling

Fig. 4A–F Three-dimensional reconstructions of the (A, B) preoperative, (C, D) immediate postoperative, and (E, F) 1-year followup CTs from Patient 3 illustrate lesion filling and bone remodeling. Three discrete lesions, illustrated in red, were identified preoperatively. At revision, 34% of the retroacetabular dome lesion was filled, 15% of the superior defect was filled, and 8% of the anterior lesion was filled. At 1-year followup, the retroacetabular, superior, and anterior defects

demonstrated 23%, 9%, and 24% new mineralization, respectively. Because new mineralization predominately occurred at the margins of the original defect volumes, the remodeled volumes (yellow) appear deceptively large in the three-dimensional reconstructions. (A, C, E) These images simulate views from a perspective perpendicular to the face of the cup; (B, D, F) these images simulate the perspective associated with an anteroposterior pelvic radiographic view.

Fig. 5A–F A series of registered CT slices from Patient 5 demonstrate postoperative bone remodeling is related to lesion filling at the time of revision. (A) The preoperative slice includes portions of two osteolytic defects defined by the yellow regions in (B). (C) A slice from the immediate postoperative CT demonstrates substantial filling of one defect and very little filling of the other defect in this particular

image slice. (D) The lesion filling is identified as the red region and the original defect area as the yellow region. (E) At 1.4-year followup, the portion of the lesion with more filling at the time of revision demonstrates increased mineralization compared with the defect with very little filling. (F) New mineralization is identified as the red region and the original defect area as the yellow region.

Fig. 6 Postoperative filling and followup mineralization data indicate bone remodeling was directly proportional to defect filling at revision. Although the trends are similar, the data derived from below the level of the cup demonstrate more variation owing to the metal artifacts than the artifact-free data from above the cup. The regression line, based on the artifact-free data, reveals bone remodeling at 1-year followup was approximately 1/2 (47%) of the filling achieved at the time of revision. Defects that were not grafted tended to remain static without evidence of new mineralization. Owing to metal artifacts, small or untreated defects inferior to the cup could demonstrate negative filling rates.

and new mineralization data from the artifact-free region above the cup and the region with artifact at and below the level of the cup reflected similar trends. Using the data obtained from the artifact-free regions above the cup, the percentage volume of new mineralization at 1-year followup was proportional ($r^2 = 0.70$, $p < 0.001$) to the percentage of the defect volume filled with graft on the immediate postoperative CT (Fig. 6). No pelvic fractures were noted at followup and all cups remained stable.

Discussion

Although the timing of intervention and preferred treatment strategies for the management of osteolysis differ among orthopaedic surgeons, there is agreement that preservation and restoration of host bone stock are always desirable [1, 21, 25, 36]. However, quantifying bone remodeling using conventional radiographs is difficult (Fig. 2). The objective of this study was to develop a technique that could be used to measure three-dimensional bone remodeling while minimizing the subjective nature of the analysis. Using clinical CT images, we have proposed a method to quantify new bone mineralization within osteolytic lesions. To illustrate the application of this technique, we have presented pilot data using one type of bone graft substitute.

Although we attempted to minimize the use of subjective assessments, our method is limited by the fact that it requires the reviewer to define several specific regions during the analysis process. When calibrating each CT image, the analyst must define each of the rods within the phantom. This is relatively easy because the rods have a

well-defined geometry and can be readily distinguished within the phantom (Fig. 1). We routinely define the rods slightly inside their apparent boundary on the CT slices to avoid partial voluming effects near the edges. To match CT images taken at different times, the analyst also must define the portions of the bone used for registration. To do this, we routinely select the entire pelvis above the cup since this bone is artifact-free. Once the region to be used for registration has been defined and the images are roughly aligned by the reviewer, the analysis software optimizes the image matching via registration. The quality of the match can be confirmed by visually inspecting the inferior portions of the pelvis not used for registration. This technique can be used regardless of whether the cup is retained or revised, since it is based on the pelvis. When the metal shell is retained, inspection of the superimposed images after registration also readily enables determination of any cup migration. In the third step of our method, the analyst must define the osteolytic lesion and a region to evaluate trabecular bone density. Owing to residual metal artifacts and the fact that osteolytic lesions do not always have well-defined continuous borders on all CT slices, we have been unable to automate the detection of osteolysis. However, the reviewer is only required to trace the osteolytic lesion volume on the preoperative CT. Once this is done, we use image registration to analyze the exact same region on all CT images for a particular patient. A major advantage of our technique is that it eliminates the need for a reviewer to trace the residual defect regions, grafted regions, and remodeled bone on the immediate postoperative and followup CT images. The region corresponding to the original osteolytic lesion can display heterogeneous changes in density and no longer has a well-defined volume devoid of

bone similar to the pretreatment defect (Fig. 3). As a consequence, manually defining the residual lesion volume after revision with grafting can be quite difficult and subjective. To establish a patient- and time-specific threshold for trabecular bone, our technique also relies on the reviewer to establish a region within the iliac crest to assess bone density. In the same way we evaluate remodeling using the exact same regions on each CT, we also evaluate bone density in identical locations using image registration. Thus, the analyst does not define the density threshold for trabecular bone but chooses the region where the analysis software evaluates the bone density based on the calibrated image data. The subjective part of this step relates to the fact that the reviewer must select a relatively uniform region, devoid of cysts or dense regions of ossification, representative of the patient's trabecular bone. Once a patient-specific threshold for trabecular bone is established, the process of evaluating what happens within the osteolytic lesion volume does not require the analyst to trace regions they subjectively determine to demonstrate evidence of bone remodeling. Instead, the image analysis software automatically classifies each voxel within the osteolytic lesion volume. In the event the preoperative osteolytic lesion volume defined by the analyst includes any voxels with densities above the patient-specific trabecular bone threshold, these portions of the image will be classified as mineralized regions by the image analysis software and accounted for when we compare CT images to evaluate bone remodeling at different time points. By using a patient-specific threshold for trabecular bone and employing the image analysis software to consistently impose this criterion, our analysis technique reduces observer subjectivity. This method also enables us to accommodate variations in bone density among different individuals, potential changes in global bone density that may occur over time during the followup period, and differences among CT machines. In summary, manual tracing where the analyst must carefully discriminate a border is limited to the identification of the osteolytic lesion volume on the preoperative CT image. Although our method requires the analyst to define several other regions, the borders for these regions are not critical and other more automated tools within the software application can be used for these tasks.

Several other limitations of this study should also be considered. First, we have used the term "mineralization" instead of "bone remodeling" in the Results section to characterize our pilot data since CT cannot be used to determine the viability of mineralized regions. However, because the calcium sulfate-based graft material appeared to have completely resorbed by the time of the 4-month followup radiograph, we suspect mineralized regions within the original osteolytic lesion volume at 1-year followup

represent new bone formation. Since new mineralization was frequently pronounced in regions where the calcium sulfate graft had not been injected, this seems reasonable. However, we do not have evidence that the mineralized regions demonstrated metabolic activity representative of viable bone. Second, because these data cannot be compared to other graft materials or surgical techniques without additional research, we cannot make any conclusions about the comparative efficacy of the surgical technique and bone graft material we used. As a consequence, it is not our intention to advocate any particular method for treating osteolysis based on the current data.

Given the current state of technology, the method we have proposed would be cost-prohibitive in a purely clinical environment because it requires multiple CT scans, sophisticated image processing software, and a substantial amount of time to complete the analysis. Additional research to automate the process of defining the preoperative osteolytic defect volume and validate the trabecular bone density in the iliac crest is representative of the periacetabular trabecular bone density would also be useful. However, as a research tool, our technique has the potential to quantify the results of different osteolysis treatment strategies in a far more objective way than methods relying on conventional radiographs. Because the treatment strategies and the grafting materials used to manage osteolysis can be expensive, the ability to quantify the performance of different techniques and substances could provide potential savings by improving outcomes. It could also provide clinical evidence to determine the most effective bone grafting materials and treatment strategies.

The analysis technique we have developed based on serial CT images coupled with computer-assisted, three-dimensional image analysis using commercially available software offers several advantages compared to previously published techniques. Methods based on plain radiographs suffer from the inherent inability to quantify three-dimensional changes in bone density. Plain radiographs also make it difficult to definitely identify osteolysis and can lead to overestimation or, more commonly, to underestimation of defect size [20, 32]. The complex geometry of the pelvis, with cortical bone superimposed on trabecular bone in plain radiographic images, also makes it particularly difficult to evaluate changes in trabecular bone density where osteolysis typically occurs. The sclerotic margins of the osteolytic lesions are often the distinguishing features on radiographs and atrophy of these borders can create the impression of defect healing on radiographs even though there has been no actual change in the surrounding trabecular bone. Calibrating and normalizing each image with respect to known densities using a phantom also avoids the problems associated with radiographs taken at different exposures. Previously published

CT-based techniques have required carefully controlled patient positioning during imaging and analysis of bone remodeling has been restricted to discrete regions above the cup [37]. Our technique does not require consistent patient positioning because it relies on computer-based image analysis to match user-defined portions of the bone that do not change from one image to another. By using registration, we can also examine and compare precisely the same regions in CT images obtained at different time intervals. Although we limited our analysis to the preoperative osteolytic lesion volume in this study, our technique could also be extended to evaluate bone remodeling in other regions. Since remodeling may not be confined to the preoperative osteolytic defect volume, our analysis technique could also be used to determine if particular treatment strategies and materials stimulate peripheral bone remodeling by evaluating changes in the host bone outside the original defect volume.

The 10 hips included in this report represent patients who were treated in a similar manner and now have 1-year followup CT images available. Nine of these hips were included in a previously published study examining the quality of osteolytic lesion filling using an immediate postoperative CT image [12]. Although we evaluated osteolytic lesion filling in both studies, we used different techniques. In the previously published study, the osteolytic defect and the volume of graft material filling the lesion were manually traced. In this study, a different reviewer traced the preoperative defect volume and image analysis software was used to calculate defect filling on the immediate postoperative CT by automatically detecting the regions within the osteolytic lesion volume having a density greater than the patient-specific trabecular bone threshold. Because the bone graft substitute we used was much denser than trabecular bone, it was relatively easy to manually trace the filled regions, and the defect filling among the nine hips with 19 discrete osteolytic lesions common to both studies was quite similar, averaging 41% for the current study and 47% in our previous publication. However, the heterogeneous nature of the bone remodeling at 1-year followup made the manual tracing technique tedious and highly subjective. This observation motivated the development of the more automated technique proposed in this study.

The radiographic analysis technique we have developed enables the evaluation of three-dimensional mineralization and can be applied to any treatment method. If a revision is performed, it provides a method to quantify the effectiveness of surgical techniques and the response to bone graft materials or other orthobiologic agents used with the intention of supplementing host bone. Although the pilot data presented in this study should be regarded as preliminary, it offers several interesting insights. Because new

mineralization was directly proportional to defect filling, we continue to make every effort to maximize defect filling at revision. Data from other materials would be required to determine whether this conclusion could be generalized. Notably, we found osteolytic lesions that were not débrided or grafted had negligible amounts of new mineralization at 1-year followup. Although these untreated defects demonstrated very little, if any, evidence of new mineralization, they also demonstrated no evidence of growth at 1-year followup. Longer followup will be required to determine how bone remodeling progresses over time.

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