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OF OSTEONECROSIS**

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**A SEMIAUTOMATED VOLUMETRIC DESCRIPTION OF
OSTEONECROSIS**

(Correlation with factors associated to etiology)

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Abstract

A semiautomated volumetric feature extraction method is presented for the extraction and measurement of the affected volume in osteonecrosis from Magnetic Resonance Imaging (MRI) scans of the human femoral head. The technique is based on the definition of an equivalent sphere model for the femoral head. The technique can be used to spatially describe the size, location, configuration of distribution of a necrotic lesion into the femoral head. In this work we study the influence of the mechanical and the different etiology associated factors.

1. Introduction

A number of studies have indicated that the site and extent of the necrotic lesion affect the fate of osteonecrosis of the femoral head, due to the different loading conditions on the superior, anterior and medial segments of the articular surface, compared to their opposing sites. The currently used radiographic techniques to quantitatively assess the osteonecrotic segment, present significant limitations, because they reveal only the inorganic component of the affected bone, whereas osteonecrosis primarily affects bone marrow. In addition, the spatial three-dimensional description of the lesion is not accurate on a two-dimensional image, such as the X-ray film. It is imperative that a new methodology to describe the lesion be established. Most authors agree that a universally accepted classification should be based on the more sensitive and specific MRI images. Obviously, a 3D representation of the size, location and distribution of the necrotic lesion allows more accurate evaluation of the severity, better prognosis and will facilitate treatment selection, and outcome evaluation.

MRI is now well established as the most sensitive and specific tool, in that it can early detect the reparative process to necrosis, between one week and one month after the initial ischemia and is much more sensitive than X-ray methods, including Computerized Tomography.

Since the anatomical limits of the femoral head are not uniform among the individuals, the difficulty in expressing the percentile affected by avascular necrosis is addressed through the introduction of the concept of the sphere equivalent. The sphere equivalent of the femoral head is defined as the sphere with the smallest radius that encloses the femoral head.

The purpose of the study was to spatially describe the size, location, configuration and distribution of a necrotic lesion into the femoral head, using digital image processing techniques with a reproducible method to quantitate data obtained from MRI films. The influence of the mechanical and the different etiology associated factors was further investigated.

2. Materials and Methods

In a cohort of 50 patients referred to us with symptomatic osteonecrosis of the femoral head, for surgical treatment, thirty five patients were male and fifteen female. Preoperative MRI revealed 81 affected hips. The etiology associated factors are listed in Table 1, with the corresponding numbers of patients and hips affected. The mean age for the study group was 31.5 yrs and for each etiology related subgroup is listed also in Table 1. Serial MRI cuts in T1 and T2 weighted sequences, of these hips taken at an increment ranging from 2 to 10mm (mean: 5.13 mm), in coronal, sections were used to reconstruct the 3D images with the method described below.

The MRI slices were digitized with a VIDAR VXR 12 scanner (Vidar Systems Corporation, Virginia, USA). All data were entered to, and measured on a SUN Sparc5 workstation (Sun Microsystems, California, USA) using the ANALYZE Version 7.5 image analysis software (Mayo Foundation, Minnesota, USA). Digitized MRI images are shown in Fig. 1. The affected region was defined as the region with abnormal signal and was outlined for each MRI slice, using the tracing tool of the ANALYZE software. Then the smallest circle that circumscribes the femoral head was found. If there was flattening of the articular surface, its normal contour before collapse was reconstituted for each MRI slice, by using the smallest circle that circumscribes the unaffected part. Using the radial divider tool of the software, the

circle above was divided in four and the area of the affected region corresponding to each quadrant was measured, (Fig. 1). In the first column those images are given without any processing and in the second column after processing. The circle describes the femoral head area for the certain position, and the affected area has already been detected (green area).

For each case the central slice (largest section), from the MRI phantom is chosen and the sphere equivalent of the femoral head is constructed based on an area measurement. The volume of the sphere was calculated in mm^3 using the data on the MRI slices. For each MRI slice the radius of the circle can be easily detected as it is shown in Fig. 2a. A much better representation of the sphere equivalent is given in Fig. 2b, where the reconstructed three-dimensional femoral head is shown, with the affected area stained darker.

For orientation purposes, making use of quadrants to localize the lesion was too crude, so octants were used. The sphere equivalent is divided in eight parts (octants or half a quadrant) with three planes (coronal, sagittal and transverse) that intersect at the center of the sphere (Fig. 3). The abbreviations in Table 2 are used to describe each octant and will be used from now on. For the computation of the volume affected a simple Simpson's rule is used to integrate in the x direction. The total affected volume per octant is computed by:

$$V_{tot} = \sum_{n=1}^N A_n d_n \quad (1)$$

where n is the MRI slice, A_n is the affected area of the MRI slice and d_n is the distance of the n-th slice from the previous one. In the above process the slice

thickness has been ignored since the average of the affected surface is taken. Finally, the affected percentage per octant is computed as:

$$\alpha = \frac{V_{tot}}{\left(\frac{1}{6}\pi R^3\right)}. \quad (2)$$

The extent of the lesion is expressed as the percentage of the corresponding octants affected. Although the absolute value of the volume of the lesion and the sphere equivalent could be measured, it was more convenient to work with proportions due to the difference in size of the femoral heads among the individuals.

All the data obtained from the measurements were processed and expressed for the size of the lesion in each subset according to the etiology, the location of the affected segments in the quadrants and further more the distribution of the lesion in each octant. Statistical analysis between different etiologies was carried out by one way ANOVA and pairwise comparisons were then performed with LSD test. The comparison among segments was performed with student t-test for Dependent Samples.

3. Results

From the 81 affected hips, 67 were symptomatic at the time of their initial examination. In the subset of patients with bilateral disease only 55% had symptoms on both hips. The remaining 14 hips were silent at the time of the initial presentation of the patients, and were diagnosed on the MRI examination. In 6 out of the 50 patients, MRI examination demonstrated necrotic lesions in ten shoulders.

Size of the lesion: The affected part ranged from 17.04 % to 25.39 % of the sphere equivalent of the femoral head, the overall mean was 21.26 % (± 11.03). In the

subgroup of patients with osteonecrosis associated to excessive use of alcohol and to those with history of hip trauma, the mean size of the necrotic part was 25.39 % (± 12.1) and 25.30% (± 14.0) (group 1, n = 23 hips). In the femoral heads from patients with previous use of steroids and those under immunosuppression, the average size of the lesion was 21.29% (± 9.1) and 19.93% (± 12.01) respectively, (group 2, n = 40 hips) and in group 3 with patients suffering from Systemic Lupus Erythematosus (SLE) and those with idiopathic osteonecrosis n = 18 hips, the average size of the lesion was 18.65% (± 8.2) and 17.04% (± 8.5) respectively (Fig. 4).

Distribution of the lesion: The octants derived from the intersection of the three planes-coronal, transverse and sagittal, at the center of the femoral head. Measurements of the size of the affected part into each one of the octants demonstrated that the most extensively affected was the ASM in which the mean size of the necrotic segment was 53.85% (± 23.5) of the octant. The necrotic segment varied from 46.21% (± 20.8) in patients under immunosuppression, up to 63.80% (± 23.8) in patients with alcohol related necrosis. The second most affected octant was the ASL with mean size of necrotic segment 36.46 % (± 22.3), ranging from 29.2 % to 51.93 %. The PSM octant is the third most affected with overall mean 35.0 % (± 21.4), ranging from 31% to 39.6 %. The PSL octant follows in decreasing order with mean size 19.98 % (± 19.4), ranging from 10.3 % to 25.7 %. The two anterior-inferior octants, AIM and AIL had 11.8 % (± 16.1) and 6.08 % (± 10.9) mean values respectively (range 5.7 – 20.5 % the former and 0.8-14.6 % the latter). The mean values for the PIM and the PIL were 4.5 % (± 9.0) range 4 –7 % , and 2.29 % (± 6.0) range 0.7-3.9 % respectively (Figs. 5 and 6).

The influence of the different etiology associated factors on the configuration of the lesion was examined comparing pairs of octants. The ASM octant presented

comparable size lesions in all etiologies except in the subgroup of patients receiving immunosuppression, demonstrating significantly smaller necrosis ($p < 0.03$ - LSD test and independent t-test). In contrast, the ASL octant presented with variable size lesions, as patients with osteonecrosis from alcohol and hip trauma had significantly larger lesions inside this particular octant compared to the other etiology subgroups ($p < 0.038$).

Examining the sizes of the necrotic segments into each hemisphere of the sphere equivalent of the femoral head, we created the following combinations according to the sectioning plane (statistical analysis with t-test for dependent samples). The medial half was more severely affected compared to the lateral half, ($p < 0.0000$). The upper hemisphere was constantly found much more extensively affected compared to the inferior hemisphere ($p < 0.000$). Similarly, the anterior half had larger lesions compared to the posterior ($p < 0.000$).

Inside each hemisphere there was also asymmetrical involvement. In the superior hemisphere of the femoral head, the medial half of it, included larger lesions in comparison to the lateral, in all the etiology related subgroups. The size of the necrotic segment into the superior-lateral half presented with greater variability unlike the other quarters. In cases related with the use of alcohol, steroids and injury, the lesions were significantly larger compared to the other etiologies ($p < 0.04$). In the inferior hemisphere the lateral half was the least affected (Fig. 6a).

Dividing the femoral head in the coronal and the saggital plane the deriving quadrants were affected in the order presented in Fig. 5a. All the quadrants presented non-significantly different lesions among the etiologic factors, except from the anterior-lateral quadrant in which alcohol and trauma caused significantly larger damage ($p < 0.04$).

4. Discussion

The clinically observed relationship between the radiographic appearance of the necrotic lesions in the femoral head and clinical outcome, has been associated to differences in the structural compromise between patients, related to the extent and configuration the affected subchondral bone. Small lesions, away from the articular surface, have a more benign natural history if left untreated, in contrast to the very rapid deterioration of large lesions extending to the subchondral bone of weight bearing regions, either treated or not. We attempted volumetric description of the affected bone of the femoral head, from serial MRI tomograms processed with modern image processing techniques. The actual size of each lesion was measured and expressed as the percentile of sphere equivalent of the femoral head, thus normalizing individual size differences between patients. The precision and the accuracy of the measurements is related to the magnitude of the available data obtained from MRI, i.e. the number of slices, the increment of sections and the completeness of the study in all orientations (i.e. coronal, transverse and saggital). The overall mean size of the necrotic bone was about one fifth of the sphere. Posttraumatic necrosis and those associated to alcohol abuse caused larger ischemic insult to the subchondral bone, followed by the use of steroids, immunosuppressive treatment and the presence of SLE. Idiopathic osteonecrosis demonstrated the smallest lesions.

The pathologic bone was invariably located towards the medial, superior and anterior regions of the femoral head. In cases with more advanced stage, collapse was also present in the same locations. These observations are consistent with the biomechanically determined loading conditions at the corresponding articular surface.

The resultant joint loads from the acetabulum to the femoral head are always directed inferiorly, laterally and posteriorly. These directions do not change throughout routine activities regardless of hip orientations. Most authors suggest that the various etiologic factors finally act through a common pathway exerting an ischemic insult on a certain region of the femoral head. The uniform appearance of the lesions into the same superior, medial and anterior segments, is emphasizing in particular the role of the mechanical environment underneath the articular surface of the femoral head, as a major determinant of the location osteonecrosis is established. The different etiological factors examined in the study did not apparently influence the location of necrosis, but they markedly affected the size.

In contrast to the constancy of the location the femoral heads were affected, there was a considerable variation in the size and the distribution of the pathologic bone throughout its different segments. The pathologic bone into the anterior-lateral quadrant presented significant variability among the different etiologic factors, with trauma and alcohol causing significantly larger lesions into this particular segment. Similarly for the superior-lateral quadrant, the lesions were larger in the subgroups of patients in which osteonecrosis was related to trauma, use of steroids and alcohol overuse. These findings coincided with the propensity of the same etiologic factors to cause larger lesions. Thus the variability of the size of the necrotic region is directly related to similar variability in the distribution of the pathologic bone, preferably, towards the superior-lateral and anterior-lateral segments of the femoral head. This finding is emphasizing the prognostic value of accurate assessment of the configuration and distribution of necrosis, as from clinical observation and a number of reports, lesions extending beyond the lip of the acetabulum are more susceptible to collapse compared to those contained medial to its limits. In narrow medially located

lesions, a lateral pillar of intact bone is stress shielding the pathologic segment from loads exceeding its ultimate strength.

The accuracy and precision of the methodology employed in this study depends on a number of factors such as the quality of the MRI imaging, the quantity and the orientation of the available sections, the image processing methods followed, the presence or absence of collapse and the use of appropriate hardware and software. As much as the latter is improving and is becoming user friendly, the described technique may provide the treating physician with a valuable tool for more accurate assessment of the size, location, configuration and distribution of the necrotic lesion into the subchondral area of the femoral head. This may allow for better patient selection for the given treatment options, better prognosis, as well as the evaluation of the results of the treatment. The method cannot be, at this stage, fully automated since the physician has to determine the sphere equivalent. This arbitrarily selected means of expressing our measurements gives certain advantages such as overcoming the problem of determination of the boundaries of the femoral head and normalizing the anatomical differences of the femoral head among individuals. Utilizing the three standard planes, i.e. coronal, saggital and transverse, intersecting at the center of the sphere, the distribution of the lesion between hemispheres, quadrants or octants is more accurately and precisely measured. In previous reports, other researchers in the field have attempted to quantify the osteonecrosis. Koo and Kim proposed measurement of angles on MRI slices. In Steinberg's as well as in ARCO's classification, both recognizing the importance of measuring the size of necrosis in scaling the severity of the disease, propose the use of angles on either MRI or X-ray images for quantification in percentiles, of the femoral head. But the major problem in all attempts for quantification using non descriptive measurements on one plane, is

the lack of accuracy and the low reproducibility in describing the three-dimensional configuration of the necrotic region, on one or two projections on radiographs or MRI slices. In the clinical practice nowadays, in dealing with patients affected from osteonecrosis, MRI imaging is a routine, either in establishing diagnosis and involvement of one or both hips or grossly assessing the extent of the lesion. In an extensive review of the imaging modalities for osteonecrosis we did not find an accurate descriptive tool for quantification, employing the wealth of data provided by the serial MRI tomograms.

In conclusion the proposed methodology offers an advanced imaging tool for quantification and volumetric description of osteonecrosis with accuracy for the size and the configuration. All lesions were consistently located in anterior, medial and superior areas, underneath the major resultant joint forces. The distribution and three-dimensional orientation of the pathologic bone in the subchondral area, is also precisely described. Certain etiology associated factors such as alcohol, trauma and steroids exert larger damage on the femoral head, extended towards the superior and anterior-lateral sites, probably influencing prognosis. The method allows the formation of an electronic database, available not only to the researchers but also valuable to the treating physicians. It is continuously under development in order to become simple, more user friendly and expandable into other locations where necrosis is established in the skeleton.

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Figure Legends

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- Figure 2a: Femoral Head Sphere Equivalent.*
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- Figure 9: Volume Affected for Each Etiology by Octant (%).*

ASL	Anterior Superior Lateral	PSL	Posterior Superior Lateral
ASM	Anterior Superior Medial	PSM	Posterior Superior Medial
AIL	Anterior Inferior Lateral	PIL	Posterior Inferior Lateral
AIM	Anterior Inferior Medial	PIM	Posterior Inferior Medial

Table 1: Octant Abbreviation.

Number of patients: $n = 50$, Number of Hips: $n = 81$,
 (Right hip: 10, Left hip: 9, Bilateral: 31)

<i>Etiology</i>	<i>Patients</i>	<i>M</i>	<i>F</i>
Alcohol	11	11	0
Corticoid	10	9	1
Idiopathic	7	5	2
Immunosuppression	12	5	7
Injury	6	4	2
SLE	4	1	3

<i>Stage</i>	<i>Patients</i>	<i>M</i>	<i>F</i>
Pre-collapse	5	2	3
Crescent Sign	17	13	4
Post-collapse	28	32	8
Total	50	35	15

Table 2: Patient Description according to Etiology and Stage.

<i>Etiology</i>	<i>Hips</i>	<i>M</i>	<i>F</i>	<i>Mean Age</i>
Alcohol	16	16	0	33
Corticoid	17	15	2	36
Idiopathic	10	7	3	29
Immunosuppression	23	10	13	29
Injury	7	4	3	32
SLE	8	2	6	25
Total	81	54	27	

Population Age Average: 31.5 years		
	Average	Range
M	33	17 to 54
F	28	17 to 49
MRI Slices: Coronal 50, T ₁ and T ₂ weighted. Mean gap 5.13 mm (2 to 10mm)		

Table 3: Hip Description according to Etiology and Stage.

























