Normal microscopic architecture of acetabular labrum of hip joint: a qualitative original study with clinical aspects

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Summary

Background: Normal histologic architecture of acetabular labrum, regarding presence of Free Nerve Endings (FNEs) and Nerve End Organs (NEOs) has been four times described. Nevertheless, elderly cadaveric specimens and individuals were recruited, leading to considerably high unreliability probability due to microscopic degenerative alterations. Aim of this paper is to analyze distribution pattern of FNEs and NEOs in acetabular labra of healthy middle-aged individuals, configuring thus more reliably acetabular labrum microscopic profile.

Materials and methods: Six patients with middle age 52 ± 2.5 years were enrolled in this study. Injury of acetabular labrum and normal hip radiograph were present in all cases. Patients were all subjected to successful hip hemi-arthroplasty and derived acetabular labra were subsequently histologically processed and observed under a compound microscope.

Results: FNEs and NEOs were detected in all specimens. All types of NEOs were identified, including Paccini, Golgi-Mazzoni, Ruffini and Krause corpuscles. FNEs and NEOs were both in ventral part and in chondral side of labrum predominantly detected.

Conclusion: FNEs and NEOs presence was greater in ventral side of labrum, being thus in partial agreement with previous studies results. Further study is required, in order to elucidate the exact acetabular labrum normal microscopic anatomy.

Level of evidence: IV.

KEY WORDS: acetabular labrum, free nerve endings, histology of acetabular labrum, nerve end organs, original article, review.

Background

Acetabular labrum of hip joint constitutes a fibrocartilaginous ring, circumferentially adherent in acetabular rim. Functionally, labrum contribution to hip joint stability is well established. The first chronologically reported microscopic investigation and description of FNEs and NEOs in acetabular labrum is attributed to Kim and Azuma¹, who identified these structures, emphasizing in their possible involvement in nociception and proprioception.

Physiologically, FNEs are responsible for the detection and transmit of pain sense to cerebral cortex (nociception), while, NEOs function features great variability; detection and transmit of stimuli associated with touch (Merkel’s disks), light touch as well as vibration (Meissner’s corpuscles) and, furthermore, deep pressure and vibration (Golgi-Mazzoni corpuscles, Paccini corpuscles and Ruffini corpuscles). NEOs are consequently functionally related with proprioception.

Presence of FNEs and NEOs in acetabular labrum of normal hip joint has been described three times¹-³, being additionally specially analyzed within a general review on neural anatomy of hip joint⁴. Results present a relative diversity among the studies. However, in all studies, acetabular labra were derived from elderly, featuring thus microscopic degenerative alterations.

To our best knowledge, this is the first study of microscopic architecture of acetabular labrum of hip joint conducted harvesting acetabular labra without imaginary degenerative characteristics. Aim of this original
study is to report the distribution pattern of FNEs and NEOs in acetabular labrum of normal hip joint with greater reliability from previous studies, as elucidated in our own histological evidence. Furthermore, a short review of the literature is performed, comparing our qualitative results with those of previous studies. Exact histological architecture of normal acetabular labrum may be therefore illustrated, enabling thus better understanding of its microscopic anatomy, as well as its versatile role in hip biomechanics and in pathogenesis of degenerative diseases (e.g. osteoarthritis).

Materials and methods

This study was conducted in Department of Orthopaedic Surgery, Amalia Fleming Hospital, Athens, Greece. A total of six patients were recruited in the study, with mean age 52 ± 2.5 years old. Inclusion criteria involved acetabular labrum injury with normal hip radiograph. Patients mentioned in medical history neither osteoarthritis, nor the presence of any systematic diseases or ailments that could affect musculoskeletal system. After detailed explanation of requirements and aims of this study, complete acquiescence of all patients was accomplished. Study was clearly according to the ethical standards of the Journal conducted. Subsequently, successful hip hemi-arthroplasty was performed, and acetabular labrum was derived for macroscopic observation and histological investigation.

Macroscopic observation of acetabular labrum revealed no anatomic or degenerative abnormalities (Fig. 1). Histological evaluation was subsequently conducted. Acetabular labrum was anatomically partitioned in three separate parts: fronto-dorsal (posterior), middle, and ventral (anterior) part. These parts correspond to fundamentally established zone method described by Ilizaliturri et al. Ventral part corresponds to zones 1 and 2, middle part to zone 3 and, fronto-dorsal part to zones 4 and 5. Tissue sample obtaining and final results evaluation were thus facilitated. Multiple tissue samples were derived from each part, and, each obtained tissue sample corresponded in a separate labral part.

Obtained samples were maintained in -80°C and, subsequently, a cryostat (Leica CM 1500) was employed, cutting each part from dorsal to ventral plane. Horizontal cutting protocol was appointed in 200μm distance between sections. Thickness of resulting sections was 40μm. Gelatin-coated slides were utilized as supporting substrate for thaw of sections. A modified Gold Chloride Method (first established by O’Connor and Gonzalez) was conducted, for procession and staining.

Analytically, Borden’s Rea Lemon [88% formic acid admixed with 3 parts of freshly squeezed (filtered)] lemon juice placed for 15 min in dark was utilized for decalcification of obtained sections. Original tissue was then maintained in gold chloride 1% solution, after being separated from the transfused formic acid. Tissue was placed subsequently again for 10 min or its equable tint alteration to golden yellow to dark. Transfusion of Gold Chloride Solution constituted the next step, adding parallely 25% formic acid liquid solution for 30 minutes. The enriched tissue was placed in dark, maintaining room temperature. Transfusion of formic acid solution and clean and wash of the processed tissue were consecutively performed. 70% alcohol liquid solution and xylene were used for tissue washing (two times in each substance respectively). Resulting stained tissue sections were finally cover-slipped.

A light microscope (Nikon Optiphot 2) connected to a PC and a camera lucida were used for detailed histological investigation. A color 3CCD Sony DXC-950P camera and the Scion Image program aid capture of high-resolution microscopic images. Photoshop CS5 contributed to final correction of captured images.
Results

Histological observation of labral samples was performed by an expert neuropathologist, emphasizing in qualitative description of FNEs and NEOs distribution in acetabular labrum. This distribution pattern was similarly identified among the different labral parts from all patients.

FNEs and NEOs were successfully identified in all specimens derived from the 6 acetabular labra. Unmyelinated nerve fibers were considered as FNEs, being indicated with Gold-Chloride Staining. FNEs were abundant in ventral part of acetabular labrum, as identified in all specimens (Fig. 2). Presence of FNEs in middle and fronto-dorsal parts was weaker (Fig. 3), reflecting thus a greater FNEs density in ventral part. Furthermore, FNEs were detected to a greater extent in the chondral-inner side of the labrum (chondrolabral junction), featuring a significant reduction in the capsular-outer part.

Qualitatively, detected NEOs included Paccini, Golgi Mazzoni, Ruffini, as well as Krause corpuscles. NEOs distribution was remarkably similar to FNEs. All types of NEOs were basically in ventral part of labrum identified, featuring a reduction in middle and fronto-dorsal part (Figs. 4-6). NEOs density was greater in chondral side in comparison with the capsular side of the labrum, reflecting a similar distribution pattern with FNEs.

Discussion

Acetabular labrum constitutes a fibrocartilaginous anatomical structure in hip joint. Acetabular labrum is classically described as a horse-shoe shaped intra-capsular structure, adhering circuferentially to bony acetabular edge. This fibrocartilaginous adhesion is terminated in two gentle and round ends (horns), located in antero-inferior (anterior horn) and posterio-inferior (posterior horn) portion of the acetabular rim. Anterior, superior and posterior portions of acetabular rim are therefore covered by labrum adhesion. Inferior portion remains uncovered, characterized by the presence of trasverse acetabular ligament, a fibrous band merging anterior and posterior labral horns10, 11.
Anterior portion of acetabular rim constitutes an important arthroscopic landmark for determining of acetabulum clock. Acetabular labrum is internally connected to acetabular hyaline cartilage. Labrum diameters present a remarkable variety among each portion, being greater anteriorly and superiorly, featuring a gradual decrease inferiorly. Concerning hip capsule, thickness is greater in between 1 and 2 o’clock positions. Vascular supply of acetabular labrum features a significant interest. Hip capsule constitutes the primary origin, with acetabular rim be involved in to a lesser extent. Vascular density is thus greater in capsular side of labrum, enabling satisfactory healing. Gradual decrease of vascular density and supply in peripheral parts of labrum results in an avascular chondral part with a very low healing capability, in case of an injury.

Biomechanical contribution of acetabular labrum to hip joint stability is fundamental. Acetabular labrum increases, adhered to acetabular rim, surface area of acetabulum, enabling thus better articulation and providing greater stability. Furthermore, it assists hip joint, supporting 1-2% of total load applied, as confirmed during normal walking simulation. However, acetabular labrum biomechanical role is more extensive, as can be defined by study of its involvement to hip joint movements. Acetabular labrum compensates mechanical distraction forces, with possible additional involvement of translation forces. Femoral external rotation is also limited by acetabular labrum, synergistically acting with iliofermoral ligament. Injury of acetabular labrum has been related with remarkable reduction of intra-articular negative fluid pressure. Partial labral tear results additionally in joint destractive stability decrease, which is though notably improved after labrum reconstruction. Pathologic acetabular labrum seems to be thus closely related to hip microinstability and as a result, to instability and long-term osteoarthritis.

NEOs constitute fundamental microscopic structures detected in capsules, muscles and tendons. First description of NEOs is chronologically delineated in 1860, belonging to Krause. However, well-stab-
Established Freeman and Wyke NEOs classification was only in 1967 suggested, constituting the first proposed systematic NEOs classification. This classification distinguished four different NEOs types: type I, representing low-threshold and slow-adapting Ruffini and Meissner’s corpuscles; type II, representing low-threshold and fast adapting Pacini corpuscles; type III, representing low-threshold and slow-adapting Golgi-Mazzoni corpuscles, and type IV, representing high-threshold nociceptive FNEs \(^{24}\). Types I, II and III (NEOs) are related to proprioception, while, FNEs are related to nociception, representing an autonomic category.

Presence of NEOs and FNEs in normal acetabular labrum has been described four times\(^1\)\(^{-4}\). Two of these studies\(^1\)\(^,\)\(^2\) were cadaveric, utilizing cadaveric specimens for acetabular labrum histological evaluation, while, in one study\(^3\) labral specimens of patients with coxarthrosis subjected to total hip arthroplasty were utilized. Last study\(^4\) represented a review of the literature, focusing on neural anatomy of hip joint. General characteristics of these studies are provided in Table I.

Results of these studies feature a relative diversity. Kim and Azuma\(^1\) reported the presence of ramified FNEs in all specimens, utilizing twenty-three acetabular labra derived form 24 fresh cadavers with mean age 64.8 years. Furthermore, presence of all types of NEOs in all specimens was detected; Pacini, Golgi-Mazzoni, Ruffini and Krause corpuscles. It was also reported, during histological examination of a right cadaveric acetabular labrum, FNEs density was higher in superior-anterior quarter of the labrum, despite detected in all sections. NEOs were also detected mostly in superficial labral layer. However, these topographic conclusions remain doubtful due to the fact that results were based on histological investigation of only one acetabular labrum.

Gerhardt et al.\(^2\) conducted subsequently a histological investigation of acetabular labrum on 8 human cadaveric hips with mean age 76.5 years, reporting the presence of FNEs and Pacini and Ruffini corpuscles. Ruffini corpuscles were detected to a greater extent in comparison with Pacini. No information has been reported about the presence of other NEOs. Density of both FNEs and NEOs was identified to be higher in anterior part of the labrum (zones 1 and 2 according to zone method) and in periphery (chondrolabral junction).

Kilicarslan et al.\(^3\) studied microscopic architecture of acetabular labrum, utilizing labral specimens of 35 patients with coxarthrosis subjected to total hip arthroplasty. Mean age of patients was 66.4 years. This was the first study conducted on acetabular labra derived from living individuals. FNEs and NEOs were mostly in anterior labrum (description of anatomic division of acetabular labrum is similar to our study, implying thus the use of zone method) detected. However, no specific qualitative information of NEOs was provided. Simons et al.\(^4\) reported a review of neural anatomy of hip joint. Results indicated that density of FNEs was significantly higher in 10 to 2 o'clock position.

All studies concerning normal histological architecture of acetabular labrum were conducted in relatively elderly individuals. It has been reported that hip joint osteoarthritis may lead to histological architecture alteration of acetabular labrum\(^25\). Elderly cadaver selection\(^1\)\(^,\)\(^2\) may reflect this alteration, leading probably to less reliable results. In the other study\(^3\), results are more likely to be not reliable, since histological investigation was conducted on acetabular labra of hips with coxarthrosis. Review of current literature\(^4\) leads to the same relatively unreliable results.

In contrast, our study was performed utilizing acetabular labra of 6 patients undergoing hip-hemiarthroplasty due to labrum injury. Comorbidities were absent and hip radiograph revealed no degenerative alterations in hip joint. Our results may thus be more compatible with normal histological architecture of acetabular labrum, which has been by extension not adequately studied.

In our study, FNEs and NEOs were basically detected in ventral (anterior) part of the labrum (zones 1 and 2). This finding is in full agreement with these of two studies\(^2\)\(^,\)\(^3\), in partial agreement with another study\(^1\), and in full disagreement with the last study\(^4\). Kim and Azuma\(^1\) reported that presence of FNEs was

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Specimen</th>
<th>Mean Age</th>
<th>Histological Staining</th>
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<tbody>
<tr>
<td>Kim and Azuma(^1)</td>
<td>1995</td>
<td>Twenty-three acetabular labra obtained from 24 fresh cadavers.</td>
<td>64.8 years</td>
<td>Suzuki’s silver impregnation and Immunohistochemical technique for neurogenic specific protein S-100.</td>
</tr>
<tr>
<td>Gerhardt et al.(^2)</td>
<td>2012</td>
<td>8 human cadaveric hips.</td>
<td>76.5 years</td>
<td>Modified Gold Chloride Staining Technique.</td>
</tr>
<tr>
<td>Kilicarslan et al.(^2)</td>
<td>2015</td>
<td>Labral specimens of 35 patients with coxarthrosis undergoing total hip arthroplasty.</td>
<td>66.4 years</td>
<td>Immunohistochemical technique for neurofilament protein (NFP) or S-100 protein and H&amp;E staining.</td>
</tr>
<tr>
<td>Simons et al.(^4)</td>
<td>2015</td>
<td>Literature Review of 17 studies associated with neural anatomy of hip joint.</td>
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predominant in superior-anterior quarter of labrum, which is in full correspondence with ventral (zones 1 and 2) and half of the middle part (1/2 of zone 3) of acetabular labrum division utilized in our study. However, their results are doubtful as mentioned. Our anatomic division is similar with the studies that our findings are in agreement with 2, 3. It was thus reported that anterior labrum contains the highest FNEs and NEOs concentration. Anterior labrum corresponds to ventral portion (zones 1 and 2) in our division. Simons et al. 4 reported higher density of FNEs in 10 to 2 o’clock position. Results of all studies are summarized in Table II.

On the other side, results are similar among the studies in terms of comparison of FNEs and NEOs density between chondral and capsular labral portion. Kim and Azuma1 reported highest concentration of NEOs in superficial layer of labrum (chondrolabral junction). This statement was also maintained from Gerhardt et al.2, reporting that FNEs and NEOs density in higher in chondrolabral junction than in capsular portion. These results are also verified in our study. Qualitative detection of NEOs differs among the studies. Kim and Azuma1 reported the presence of all types of NEOs, including Paccini, Ruffini, Golgi-Mazzoni and Krause corpuscles. On the other side, Gerhardt et al.2 detected primary Ruffini and secondary Paccini corpuscles. The other two studies provided no information about specific NEOs detected3, 4. In our study, all types of NEOs were detected, being in full agreement with results of the first study1. Qualitative data is summarized in Table III.

To our best knowledge, this is the first study of microscopic architecture of acetabular labrum in the literature utilizing acetabular labra without any degenerative alterations, being postoperatively after successful hip hemi-arthroplasty derived. Normal histologic architecture of acetabular labrum is thus described for the first time with greater reliability in the literature. Limited number of recruited patients constitutes the main weakness of this study. Further study is thus required in order to elucidate the exact microscopic anatomy of acetabular labrum regarding distribution pattern of FNEs and NEOs.

Knowledge of acetabular labrum microscopic anatomy is essential for clinicians and surgeons. Histological alterations of acetabular labrum may occur in osteoarthritis, indicating thus a pathogenetic role of labrum25. Exact delineation of these histologic alterations during gradual osteoarthritis progress may explain clinical manifestations of osteoarthritis (i.e. pain), contributing parallelly to better understanding of osteoarthritis pathogenesis and, therefore, to development of new treatment methods. Surgical impor-

### Table II. Acetabular labrum topographic histological architecture as illustrated in the literature.

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<tr>
<th>Authors</th>
<th>NEOs topology</th>
<th>FNEs topography</th>
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<tbody>
<tr>
<td>Kim and Azuma1</td>
<td>NEOs were mostly identified mostly in superficial layer of labrum.</td>
<td>FNEs were observed in all specimens and mostly in superior-anterior labral quarter.</td>
</tr>
<tr>
<td>Gerhardt et al.2</td>
<td>Highest levels of NEOs and FNEs were identified in the anterior zone (zones 1 and 2), although they densely reside acetabular labrum.</td>
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<tr>
<td>Kilicarslan et al.3</td>
<td>FNEs and NEOs were mainly in anterior labrum (zones 1 and 2) identified, although abundant FNEs were identified in all labral zones.</td>
<td></td>
</tr>
<tr>
<td>Simons et al.4</td>
<td>No information reported.</td>
<td>Innervation is denser from 10 to 2 o’clock position of labrum.</td>
</tr>
<tr>
<td>Our study</td>
<td>FNEs and NEOs were predominantly in ventral part (zones 1 and 2) of acetabular labrum detected.</td>
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### Table III. Qualitative presence of NEOs in acetabular labrum.

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<tr>
<th>Authors</th>
<th>Identified Corpuscles</th>
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<tr>
<td></td>
<td>Paccini</td>
</tr>
<tr>
<td>Kim and Azuma1</td>
<td>(+)</td>
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<tr>
<td>Gerhardt et al.2</td>
<td>(+)</td>
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<tr>
<td>Kilicarslan et al.3</td>
<td>No specific information reported</td>
</tr>
<tr>
<td>Simons et al.4</td>
<td>(+)</td>
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<tr>
<td>Our study</td>
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tance of these findings is remarkable, enabling the topographically correct intraoperative infiltration of periarticular injections.

Conclusions
This original study indicated that FNEs and NEOs density is higher in anterior part of acetabular labrum and in chondrolabral junction. Nevertheless, further study is essential in order to adopt or reject these results. Microscopic anatomy of acetabular labrum is of paramount clinical and surgical importance, enabling better understanding of acetabular labrum pathogenetic role in hip pathology, as well as enhancing postoperative results of surgical procedures performed in hip joint.

Conflict of interest
No other relationships/conditions/circumstances that present potential conflict of interest.

References