LETTER TO THE EDITOR

Response to "Letter to the editor: Labral calcification plays a key role in hip pain and symptoms in femoroacetabular impingement"

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Dear Editor,

We are writing in reply to Dr. Zhong's comments regarding our recent publication [1]. While we appreciate the discussion and feedback, we are also concerned that some of these comments are somewhat vague and may be misleading. Our specific replies to Dr. Zhong's comments are appended below.

We thank Drs. Zhong and Ouyang for reading our work and for the discussion. We enclosed a point-bypoint response to their questions.

Firstly, we acknowledge that the lack of samples of healthy controls is an important limitation to our paper. Unfortunately, the Italian law and the IOR ethical committee do not allow for tissue sampling from donors for research purposes. So, we can obtain fresh samples from donors only in case they were not used during the operation after assignment. The same limitation was mentioned in a previous paper from our group, concerning fresh menisci from donors [2]. Concerning the present study, this issue is further complicated by the fact that samples of labrum from donors should be matched by age and sex with samples from patients with FAI. In our opinion, age-matching is a critical aspect since we believe that comparing labrum from young FAI patients with "healthy" aged donors could be misleading.

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from study. Nonetheless, our research is ongoing (we have operhad just some delay due to the COVID-19 pandemic); these aspects will be presented in an upcoming article. Concerning the second comment, Dr. Zhong's speculation is biased by the erroneous assumption that FAI (and consequently the labral tear) is limited to the anterosuperior region. We have extensively explained in the manuscript that we collected 6 cases with isolated CAM deformity, 3 cases with isolated Pincer, and 12 mixed cases. We found that labral damage was not always and not only limited to the anterior-superior region but sometimes involved the entire labrum. However, the specimens were taken by debrided labral tissues from the most damaged labral zone. We could not collect

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We should point that the FAI patients enrolled in our

study had a mean age of 33 years as opposed to 62 years

in the work mentioned by Drs. Zhong and Ouyang [3].

These significant differences in age should be considered

when trying to compare "healthy" and "FAI" labral tissues. The "physiological process" hypothesized by the

commenters could be due to aging, so it should not be present in young adults. More importantly, as clearly

stated in the abstract and throughout the manuscript,

our work focused on the association between labrum

and synovium (and other joint tissues) in patients with

femoroacetabular impingement (FAI) and the impact of

these changes on surgical outcomes. Therefore, compari-

sons with healthy tissues were out of the scope of this

multiple random samples from apparently "healthy"

zones of labrum because it was unfeasible from an

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ethical point of view. Therefore, we cannot assure that the histopathological features of the specimen correspond with the characteristics of the entire labrum.

Hubert et al. [4] stained all samples with von Kossa to confirm "calcium-phosphate deposition," and alizarin red is well-established alternative to stain "calcium-phosphate deposition" in joint tissues. We agree that the detection of BCP crystals is particularly difficult, and to distinguish BCP and CPPD, we require additional measurements, like polarized or transmission electron microscopy [5, 6]. Our ongoing studies (in collaboration with Dr. Oliviero [7]) aim to further characterize the nature of calcium deposits in FAI and OA patients, in line with Dr. Favero's (co-author in this study) expertise and research interest. We hope to report these findings soon.

Previous study stated that the amount of calcification in the labrum instead of histological degeneration grade had significant influence on the preoperative Harris Hip Score (HHS) in patients with end-stage OA [3, 4]. Therefore, how much amount of calcium crystal deposition in the labrum produce adverse effect on hip function in patients with FAI needs further study.

This is already mentioned in the Discussion "higher local concentration of calcium crystal deposition in the labrum could lead to increased release of nociceptor stimulating substances within the fibrocartilage tissue, which densely innervated" along with pertinent references. Unfortunately, the study is not powered to establish a statistically significant threshold of calcium crystals deposition in the labrum.

Sincerely, Giovanni Trisolino, Marta Favero, Enrico Tassinari, Eleonora Olivotto

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