Reviewer’s report

Title: The three-dimensional microanatomy of the chondro-osseous junctional region of the normal human knee joint.

Version: 1 Date: 24 February 2006

Reviewer: Thomas M Quinn

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General

The authors present descriptive evidence that the chondro-osseous junction in healthy human tibial plateau includes direct contacts between uncalcified cartilage and bone, via “protrusions” of uncalcified cartilage. This anatomical information is interesting and pertinent to improved understanding of cartilage function. The measurements appear to be performed accurately, but quantitative data are lacking. In the end, the Results rest upon some histological images which illustrate the contacts mentioned above, but their relative importance is not examined. Therefore the study is interesting but largely descriptive. If more effort is made in motivating the study, connecting it to existing literature, and providing more quantitative results, impact will likely be increased. Details follow in the Discretionary Revisions.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1.) Abstract and Results – “virtual islands”: it becomes clear in the course of reading the paper that these are islands of uncalcified cartilage surrounded by a sea of calcified cartilage. At least, that’s what I understood. However, this is not obvious when this phrase is first encountered in the Abstract and Results. It seems for example that the “island” is made of calcified tissue, within a sea of uncalcified cartilage. For example, in the Results, we have the sentence “Chondrocytes adjacent to these prolongations appeared … to be entombed in calcified matrix (virtual islands).” Do you mean “adjacent to” or “within”? Is the island calcified or not (vice versa for the sea)? The way this phrasing is handled throughout the paper is confusing.

Discretionary Revisions (which the author can choose to ignore)

1.) What do these findings change regarding interpretations of previous data? I was surprised that so little data was reviewed in the Intro to motivate the study. It’s not clear what difference this investigation will make if one does not see the relevant questions clearly in advance.

2.) One thing that occurred to me is that solute transport might occur from below the cartilage in addition to from the synovial fluid, as described in the Conclusions. But beyond this, biomechanical effects on transport would be different because the uncalcified protrusions would likely not deform much during tissue loading, since they are surrounded by stiffer calcified tissue. So there would be less fluid flow, and solute transport “from below” would be less influenced by compression-induced
fluid flows. Biomechanically, it’s very different, and it highlights the changing depth-dependent biomechanical environment of chondrocytes, related to the depth-dependent function of cartilage (in this case, “interfacial function”). It contrasts very strongly with the articular surface interface, where solute transport occurs in the presence of large matrix deformations.

3.) There are lots of samples used for these studies but no insights emerging from the sampling groups. Were there differences between the necropsy vs arthroplasty samples? Between men and women?

4.) No quantitative data are presented. This would require a lot more work, but this would greatly increase the paper’s likely “longevity” in the literature. What are the characteristic sizes of the protrusions (how long and how wide)? What is the volume fraction of these protrusions? Do these data change between men and women, healthy and diseased tissue, or among different joint locations (okay that’s future work)? There are stereological methods available to measure these things, and if you could attach some numbers to your observations it would be a great help to interpreting the importance and implications of your findings.

5.) Figures 8 and 9 are not easy to interpret. Furthermore, it’s not clear what they add to the study, beyond the illustrations of light micrographs already presented.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests.