Reviewer's report

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

Version: 1 Date: 16 March 2006

Reviewer: Flavia M Cicuttini

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General
This is an interesting study which suggests that chondro-osseous junction region is more complex than previously described and rather than being a straight line across a joint, is a complex 3-dimentional structure that follows uncalcified cartilage prolongations.

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

Specific comments:
1. The authors make a case that previous studies have involved human material from advanced OA and animal models. However, it is very unclear how the investigators collected their study samples. We are told that 10 necropsy cases (aged 27-70 yr) and a further 37 cases (51-83 years) were used in this study. The authors then evaluated samples which we are told were all normal. This seems rather odd in view of the generally older age, where the prevalence of knee OA is getting quite high, and the fact that the 37 cases were undergoing arthroplasty. Even if some sections of the cartilage looked normal, OA tends to be a generalized disease so could the findings be due to very earlyl OA?

2. It is not clear from the methods section how the samples from individual subjects were used in the analyses. There are no individual data shown, yet a large number of subjects were included. The methods and results sections need more detail. Are the results of one subject only? Which subjects were included or excluded? Are they composite results of all subjects? If so, was there any individual variation?

3. What effect might age, gender, possibly BMI have on the results? Could some of the changes simply be a feature of age and/ or early OA?

4. This manuscript needs a clearer description of the actual methodology and analyses so that the data presented can support the conclusions and extensive discussion presented by the authors.

5. Some consideration of alternative explanation of their results needs to be presented and also potential methodological limitations of the study.

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

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Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.