Title
Editorial comment: the future of compositional MRI for cartilage

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Editorial comment: The Future of Compositional MRI for Cartilage

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Abstract

This Editorial comment refers to the article: "Detection of early cartilage damage: feasibility and potential of gagCEST imaging at 7T" by Brinkhof et al, Eur Radiol 2018.

MRI-based cartilage compositional biomarkers, where do we stand?

In 1997 Dardzinski et al published one of the first studies quantifying cartilage T2 in young asymptomatic volunteers [1] thus establishing the concept of compositional cartilage imaging. Over the next 20 years new MRI-based techniques were developed, the techniques were validated and investigated in clinical research studies. To date the best established compositional imaging biomarkers are T_2 and T_{1rho} relaxation time mapping. Moreover, it has been shown that compositional biomarkers can assess mechanical properties of cartilage [2], predict focal cartilage breakdown [3] and also provide a risk assessment about development of radiographic OA [4, 5].

In addition to T_{1rho} and T_2 other compositional biomarkers have been developed, which include delayed gadolinium enhanced MRI of cartilage (dGEMRIC), T2* imaging, sodium imaging, glycosaminoglycan chemical exchange saturation transfer imaging (gagCEST), diffusion weighted imaging and diffusion tensor imaging. Some of these candidates, however, are unlikely going to be used clinically such as dGEMRIC (recent Federal Food& Drug administration warning concerning gadolinium storage in the body and brain for months to years) and sodium imaging (dedicated coils required and low signal to noise ratio).

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What is special about gagCEST?

Currently one of the most promising cartilage imaging biomarker candidates is gagCEST imaging, which allows to map the glycosaminoglycan (GAG) concentration in cartilage. The first feasibility study was published in 2008 by Ling et al [6] and showed that by exploiting the exchangeable protons of GAG it was possible to measure localized GAG concentrations in bovine patella samples. Subsequently the technique has been used in a number of studies [7–9] mostly at 7T. Concerns were raised about using the technology at 3T and in their experimental study Singh et al concluded that gagCEST is not expected to lead to accurate quantification of GAG content in healthy or degenerated cartilage at 3T [9]. However, the investigators conceded that the technique holds promise as a clinically viable technique at 7T.

What does the current study tell us about gagCEST?

In this issue of European Radiology Brinkhof et al use gagCEST at 7T in volunteers and patients before cartilage repair surgery to show its clinical feasibility [10]. This study is also a first step to establish this technique as an imaging biomarker. Required criteria for biomarkers include reproducibility, validity, ability to assess disease burden and to differentiate patients with and without disease, predict risk for disease and monitor therapy. The investigators developed a fast 3D gagCEST sequence and demonstrated its reproducibility scanning each volunteer two times. They found excellent reproducibility with coefficients of variation ranging from 2.25% at the lateral condyle to 1.40% at the trochlea. They also validate the measurements using findings during cartilage repair surgery as a standard of reference and they find a significantly different GAG effect in damaged cartilage compared to healthy cartilage at the contralateral condyle.

Where do we go from here?

gagCEST imaging is an exciting novel technique to better characterize localized GAG concentrations in cartilage. This study showed in a relatively small sample of subjects that the 3D gagCEST sequence developed by the investigators is reproducible and can show differences in GAG content between areas with advanced defects and healthy cartilage. While this is a promising first step, we have to consider the challenges and limitations: (i) Imaging at 7T is unlikely to become a standard clinical tool in the near future, and if this technology can not be eventually developed for 3T it will likely not be feasible for larger patient populations, (ii) a cartilage compositional biomarker needs to identify early changes of the cartilage matrix before focal defects occur and using advanced International Cartilage Repair Society grades 3 and 4 lesions for validation is not a suitable reference, (iii) biomarkers need to be comparable between different machines and vendors, and (iv) we need information on whether it can predict cartilage loss and monitor therapy. All these issuees will have, step-by-step, painstakingly, to be addressed, before gagCEST will have a future in compositional cartilage imaging. While the technique is clearly promising and the presented data are encouraging the road ahead is steep and stony.

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