In vivo quantification of arthritis-induced alterations of murine bones based on PET/CT image data

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Background

Rheumatoid Arthritis (RA)

- one of the most common autoimmune diseases
- leads to joint swelling, bone erosion,







loss of joint function

Experimental Arthritis

- used to study RA and arthritic processes
- induced by glucose-6-phosphate isomerase (G6PI) [1]

Longitudinal, *in vivo* Imaging (PET/CT)

combined positron emission tomography/computed tomography



Methods

. Prepare volumes of interest (VOIs) • extract parts of image stack

2. Reconstruct surface marching cubes algorithm [2]



CT imaging results

 arthritic animals show increased bone roughness in hind paws roughness is significantly increased already at day 10



that contain the hind paws



- 3. Calculate local roughness [3] for each facet normal
 - average angle between facet normals



triangulated surface mesh



- 4. Calculate global roughness [3]
 - composite histogram
 - sum of frequencies of angles above threshold





• variation of roughness radius *r* reveals differences between periosteal and endosteal cortical bone surface

Conclusion

- combined PET/CT imaging allows for longitudinal, *in vivo* studies
- ¹⁸F-fluoride is well suited to quantify pathological bone metabolism [4,5]
- automated CT image analysis allows for fast and objective quantification of bone destruction [4,5,6]
- roughness evaluation very sensitive for early bone erosion



- PET image analysis manually place regions of interest around paws
- calculate standard uptake value (SUV)
- revealed different dynamics of bone erosion at periosteal and endosteal sites of cortical bone



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References:

- [1] Schubert et al., (2004) Immunization with glucose-6-phosphate isomerase induces T cell-dependent peripheral polyarthritis in genetically unaltered mice, J Immunol 172(7), 4503–4509.
- [2] Lorensen and Cline, (1987) Marching cubes: A high resolution 3D surface construction algorithm, ACM Siggraph Comput Graph 21(4), 163-169.
- [3] Silva et al., (2006) Application of surface roughness analysis on micro-computed tomographic images of bone erosion: examples using a rodent model of rheumatoid arthritis, Mol Imaging 5(4), 475–84.
- [4] Irmler et al., (2014) ¹⁸F-fluoride positron emission tomography/computed tomography/computed tomography/computed tomography for noninvasive in vivo quantification of pathophysiological bone metabolism in experimental murine arthritis, Arthritis Res Ther 16(4), R155.
- [5] Hoffmann and Svensson et al., (2017) Automated quantification of early bone alterations and pathological bone turnover in experimental arthritis by in vivo PET/CT imaging, Sci Rep 7:2217. [6] Svensson and Hoffmann et al., (2017) Quantification of arthritic bone degradation by analysis of 3D micro-computed tomography data, Sci Rep 7:44434.

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