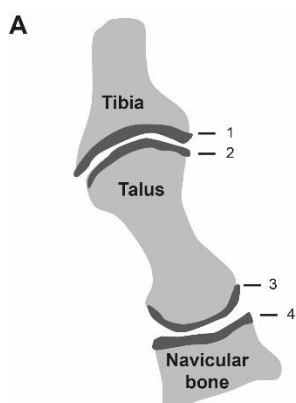


## Additional file 1

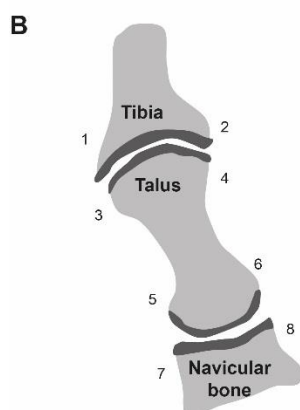


### Cartilage erosion

<b>SCORE 0</b>	no erosion, no fibrillation, cartilage surface completely smooth
<b>SCORE 0.5</b>	fibrillation / irregular surface
<b>SCORE 1</b>	mild erosion of the non-calcified layer (25% of depth of non-calcified layer)
<b>SCORE 1,5</b>	severe erosion of non-calcified layer (50% of depth of non-calcified layer)
<b>SCORE 2</b>	erosion up until the tidemark
<b>SCORE 2.5</b>	erosion beyond the tidemark, part of the calcified cartilage layer still present
<b>SCORE 3</b>	complete erosion of calcified layer

### PG depletion

<b>SCORE 0</b>	complete red staining of the superficial cartilage zone, equally stained as the deeper zone beyond the tidemark
<b>SCORE 1</b>	mild loss of red staining in the superficial cartilage zone, but still predominantly red
<b>SCORE 2</b>	moderate loss of red staining in the superficial cartilage zone, with the blue counterstaining starting to predominate throughout the remaining gloom of redness
<b>SCORE 3</b>	complete loss of red staining of the superficial cartilage zone, with only blue counterstaining remaining or absence of proteoglycans due to complete erosion of the non-calcified layer or complete erosion of non-calcified and calcified layer



### Bone erosion

<b>SCORE 0</b>	complete intact bone lining, no erosion
<b>SCORE 1</b>	superficial erosion
<b>SCORE 2</b>	deeper erosion, not yet extending to the bone marrow
<b>SCORE 3</b>	complete erosion of the bone structure, connecting the synovial cavity with the bone marrow cavity

### **Scoring system for quantification of cartilage erosion, cartilage proteoglycan depletion and bone erosion.**

Cartilage erosion was evaluated using an arbitrary score ranging from 0 (no erosion) to 3 (complete erosion of the calcified cartilage layer) in four locations (1- tibia, 2-upper talus, 3-bottom talus, 4- upper navicular bone). Proteoglycan depletion in the articular cartilage was evaluated in the same four locations as cartilage erosion and scored on a scale from 0 (no PG depletion) to 3 (complete PG depletion). In case of a complete erosion of the non-calcified layer or complete erosion of non-calcified and calcified layer, PG depletion was scored as 3, since proteoglycans are completely absent under these conditions. The score of the four locations was averaged (**A**). Bone erosion was evaluated with an arbitrary score ranging from 0 (no erosion) to 3 (connection between joint cavity and bone marrow or more extensive bone destruction) in eight locations and the score of the eight locations was averaged (**B**).