A small animal MR Elastography setup to study skeletal muscle damage and the etiology of pressure ulcers and related deep tissue injury.

Jules Nelissen[1,2], Larry de Graaf[1], Tom Schreurs[1,2], Willeke Traa[3], Kevin Moerman[4], Cees Oomens[3], Aart Nederveen[4], Klaas Nicolay[1], and Gustav Strijkers[1,2]
[1]*Biomedical NMR, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands,* [2]*Biomedical Engineering and Physics, Academic Medical Center, Amsterdam, Netherlands,* [3]*Soft Tissue Biomechanics and Engineering, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands,* [4]*Department of Radiology, Academic Medical Center, Amsterdam, Netherlands*

Target audience
(Pre) clinical scientists interested in pressure ulcer research, skeletal muscle damage, musculoskeletal MRI, and MR Elastography.

Purpose
We built an MR Elastography (MRE) actuator to study the role of tissue mechanical properties and changes therein during the development of pressure ulcer related deep tissue injury. The setup is designed to perform MRE measurements in combination with damage-inducing indentation of the tibialis anterior muscle of rats.[1]

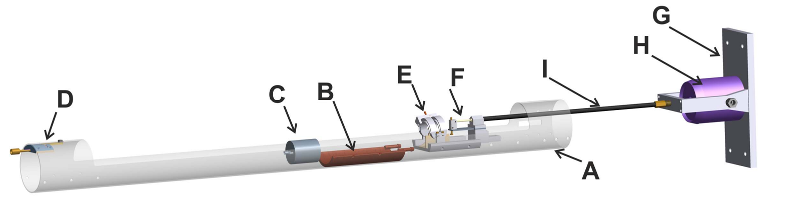

Fig. 1. Schematic representation of experimental MR compatible indentation and MRE setup.

Materials & Methods
<u>MR compatible indentation and MRE setup:</u>
The setup, schematically shown in **Fig. 1**, based on a design of Sinkus et al. [2,3,4], basically consists of (**A**) a glass fiber tube with thin 2 mm wall thickness as a rigid body to secure all parts, (**B**) a 3D printed water-circulated heating bed for maintaining the rat body temperature, (**C**) an anesthesia mask with supply and exhaust of anesthesia gas for sedating the rat, (**D**) a fixation block for the setup in the MRI scanner, and (**E**) the indentation device, to apply sustained mechanical loading to the tibialis anterior (TA) skeletal muscle in the rat. For the MRE part (**F**) a base plate (**G**) is fixed on the wall of the Faraday cage to mount an electromagnetic shaker (Brüel and Kjaer, LDS, V201) (**H**) at a safe distance of the 7T MRI magnet to set the MRE actuator (**F**) into motion via a long transmission rod (**I**). The shaker is powered with an amplifier (QUAD 50E, Huntington) and waveform generator (Agilent 33220A). Synchronization of the MRE sequence and shaker is performed via triggering. The indentation and MRE parts (**E** and **F**) of the setup are shown in more detail in **Fig. 2**. The MRE actuator can be flexibly positioned via a dovetail profile and is adjustable in height by removable plates and an adjustable MRE piston. The MRE piston is brought into motion via the drive rod attached to the electromagnetic shaker and cantilever. The indentor part designed and tested to apply sustained mechanical loading to the TA muscle of rats as described in more detail in Nelissen *et al.*, basically consists of an indentor holder on a rotatable half arch, onto which the indentor can be moved and positioned.[1]

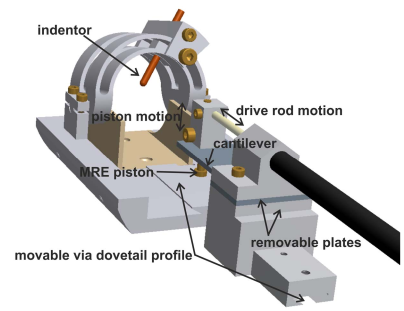

Fig. 2. Detail of indentation and MRE actuator part of setup.

<u>*Phantom test:*</u> A Bruker 7T small animal MRI scanner was used with a 3 cm diameter receive surface coil, placed on top of a 2% Agarose gel phantom in a plastic u profile, in combination with a 86 mm excitation volume coil. MR Elastography images were acquired to test the setup for MRE frequencies of 900 Hz and 1200 Hz at full gradient strength (Spin-Echo MRE, 15 coronal slices of 1 mm, FOV = 4 x 4 cm^2, MTX = 64 x 64, TE = 16.67-20 ms, 6 frames, TR = 1000.83-1001.11 ms, 9x half sine shaped MEG in slice direction, 900 Hz and 1200 Hz) and same shaker input voltage.

<u>*Rat model:*</u> 11-week-old SD rats (female, 249 - 252 gram, n=3) were measured to test the MRE part of the setup. The right leg of the rat was shaved and placed in a plastic profile filled with alginate molding substance for firm fixation, while keeping the TA muscle accessible for coupling to the MRE actuator piston.

<u>*In vivo MRI:*</u> A 3 cm diameter receive surface coil, placed on top of the TA muscle inside the indentation device, in combination with a 86 mm excitation volume coil. MR Elastography images were acquired to test the setup (Spin-Echo MRE, 15 coronal slices of 1 mm, FOV = 2.5 x 2.5 cm^2, MTX = 128 x 128, TE = 21,11 ms, 6 frames, TR = 1001,11 ms, 9x half sine shaped MEG in slice direction, 900 Hz). Anatomical and geometrical information was assessed with T1-weighted MRI. During the MRI scans isoflurane (1-2%) was used as anesthetic. Temgesic (0.05 mg/kg) was administered for analgesia.

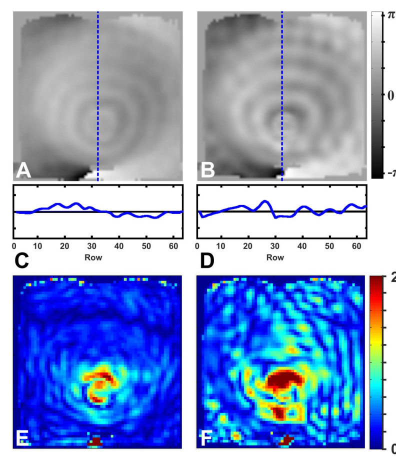

Fig. 3. MRE wave images in agarose 2% phantom. **A:** 1200 Hz MRE. **B:** 900 Hz MRE. **C, D**: 1D wave profile of blue dotted line of both wave images. **E, F**: displacement amplitude maps of 1200 Hz and 900 Hz MRE, respectively

Results and Discussion
Fig. 3 shows phantom MRE wave images of (**A**) 1200 Hz and (**B**) 900 Hz MRE frequencies. A clear difference in wavelength can be observed between the 1200 Hz and 900 Hz wave images (**C, D**). The amplitude of the 900 Hz waves is larger and waves show less attenuation than the 1200 Hz waves (**E, F**). In the 900 Hz wave image interference patterns are observed, probably due to reflection of waves on the plastic profile with which the gel was surrounded on the left and right side. In **Fig. 4** *in vivo* MRI images are shown from the TA muscle of a SD rat. (**A**) is a coronal magnitude image in which the TA muscle, tibia bone, skin, and a tendon (indicated with white arrow) could be distinguished. In (**B - G**) the corresponding MRE images are shown of the magnitude image in (**A**). Different snapshots θ of a 900 Hz MRE acquisition are shown and a propagating wave was observed. The wave had a typical v-shaped profile and showed strong attenuation. The center of the v-shaped waves anatomically corresponded to the tendon as is indicated with a white arrow in the magnitude image. V-shaped waves are caused by the faster travelling of MRE waves along a tendon.

Conclusion
An MRE actuator was successfully built for performing MRE in combination with sustained mechanical muscle loading in rats. The MRE device was successfully tested in agarose phantoms up to MRE frequencies of 1200 Hz. Proof-of-concept *in vivo* MRE measurements showed that skeletal muscle MRE is possible with the proposed MRE setup and showed characteristic v-shaped MRE waves, typical for skeletal muscle. Attenuation of the MRE waves in *in vivo* muscle is strong. Wave propagation could be lengthened by applying more power to the electromagnetic shaker or using a lower MRE frequency. We expect that the use of this MRE actuator in combination with the MR compatible indentation setup will provide new insights in the change of mechanical properties during development of skeletal muscle damage and the etiology of pressure ulcer related deep tissue injury.

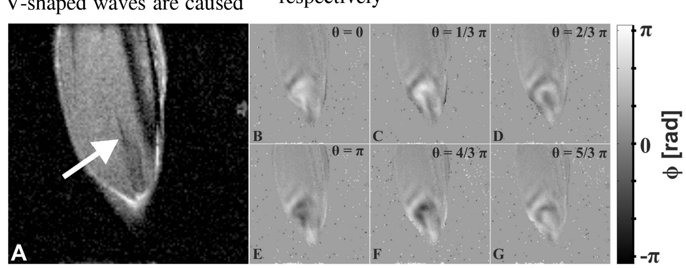

Fig. 4. *In vivo* MRE rat skeletal muscle wave images (**B** to **G**) and corresponding magnitude image (**A**).

Acknowledgement This research was supported by the Dutch Technology Foundation STW (NWO) **References**
1) Nelissen *et al.* ISMRM 2014 2) Jugé *et al.* Radiology, 2012 3) Qin *et al.* Radiology, 2014 4) Schreurs *et al.* MSc Thesis, Biomedical NMR, TU/e