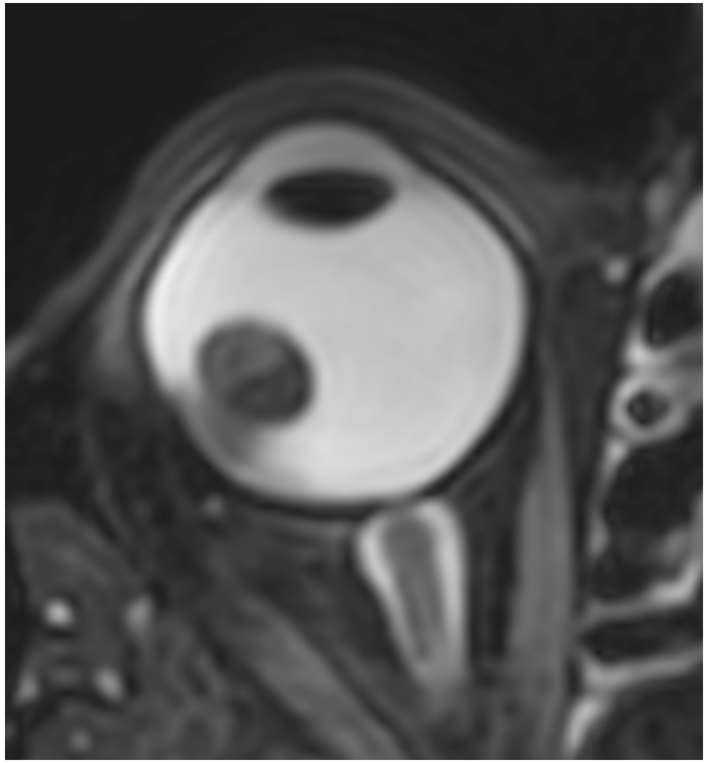
MReye



Jan-Willem M. Beenakker
Dept. of Ophthalmology, Radiology and Radiotherapy

Disclosure

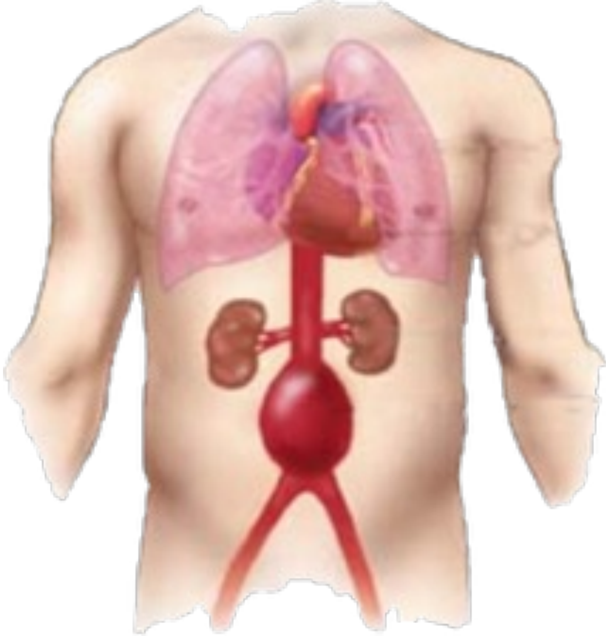
Mijn onderzoeksgroep krijgt ondersteuning van:

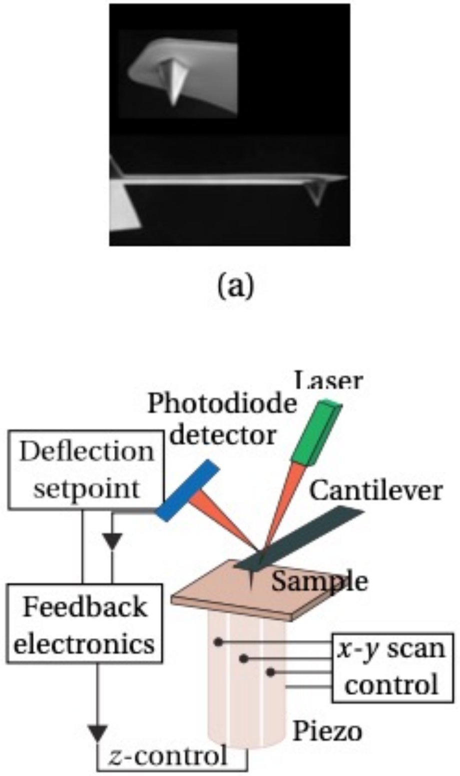
- Philips Healthcare
- RaySearch Laboratories
- Varian Medical Systems

Even voorstellen

- Jan-Willem Beenakker
- 1997-2003: Stedelijk Gymnasium Leiden (profiel NT & NG)
- 2003-2008: U. Leiden: Master in Natuurkunde (track Experimental Condensed Matter Physics)
    - 2003: Propedeuse in Wiskunde
    - Langzaam richting biofysica
- 2008-2012: PhD in Natuurkunde aan U. Leiden “Unravelling the collagen network of the arterial wall”

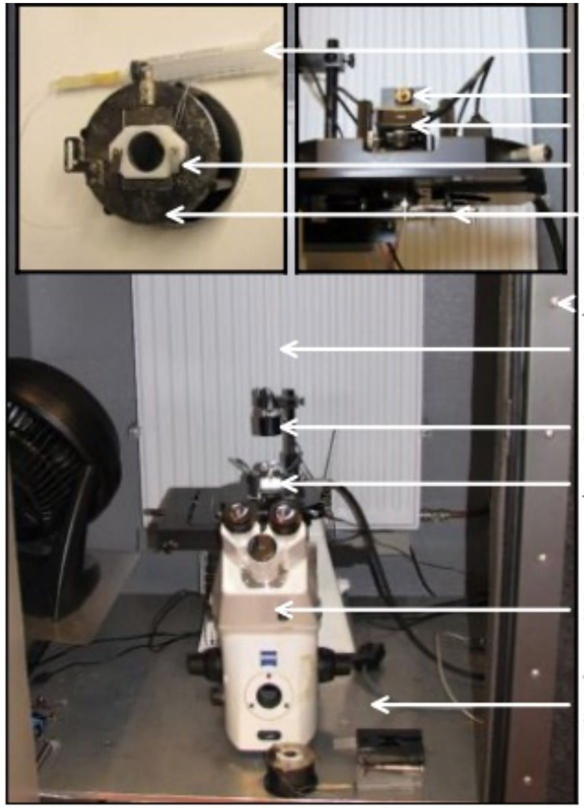
Even voorstellen



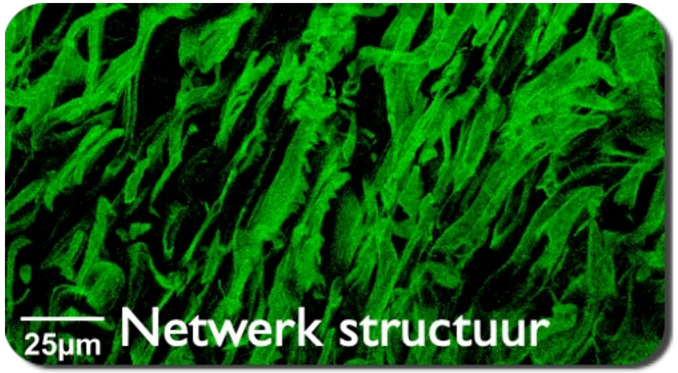


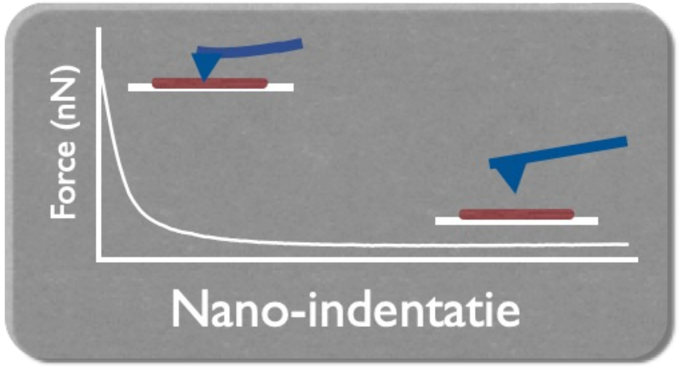
(a)

(b)



(c)





PhD supervisor prof. T. Oosterkamp

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  - 2003: Propedeuse in Wiskunde
  - Langzaam richting biofysica
- 2008-2012: PhD in experimentele Natuurkunde
- 2012: start als postdoc afdeling oogheelkunde en het C.J. Gortercentrum voor hoge veld MRI
  - Initieel project: ontwikkellen van oogMRI om zo een oogmodel te maken voor intra-oculaire lenzen
- Momenteel: Associate professor in Oogheelkunde, Radiologie en Radiotherapie
  - Zowel ”technische” als “klinische” promovendi
  - Onderzoek ontwikkelen van nieuwe oog-MRI technieken en toepassen in kliniek
    - Oogoncologie, maar ook andere oogaandoeningen

MR-fysica

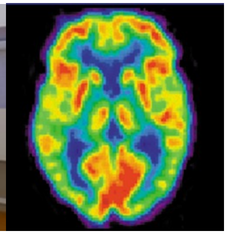
Four basic medical / biomedical imaging techniques

1. **Computed X-ray tomography**

Attenuation coefficient map


2. Nuclear medicine (SPECT, PET)

Distribution of injected radionuclide

3. Ultrasound

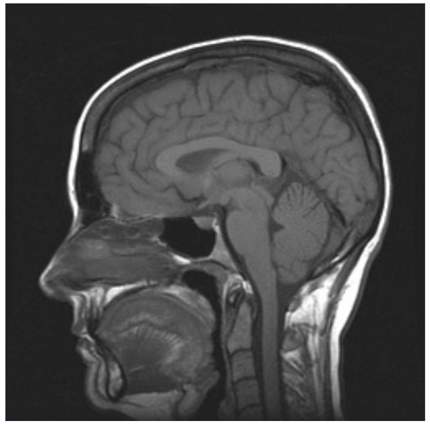
Backscattered mechanical waves


4. Magnetic resonance imaging

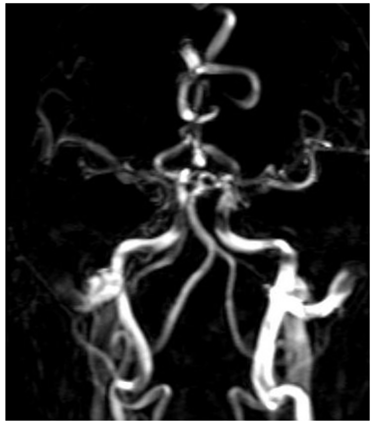
Proton (water, lipid) density, mobility


MRI: the most versatile imaging modality

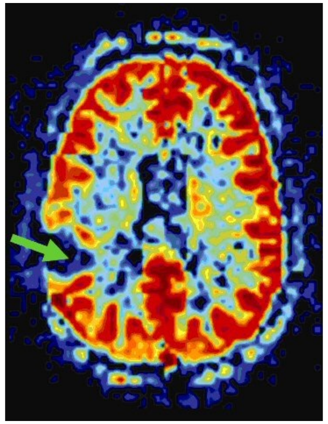
Structural



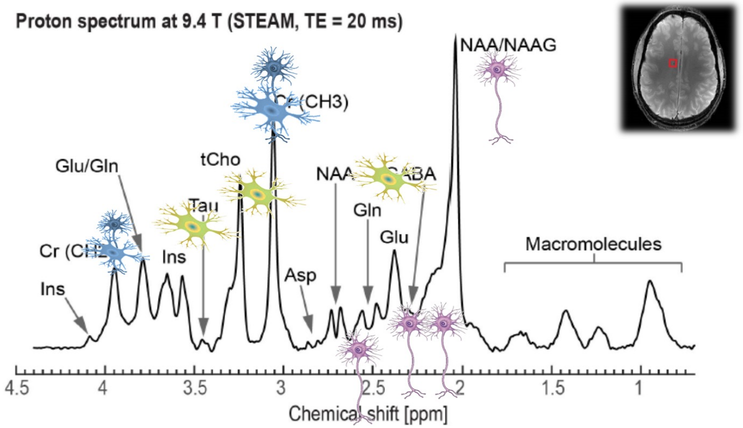
Blood flow

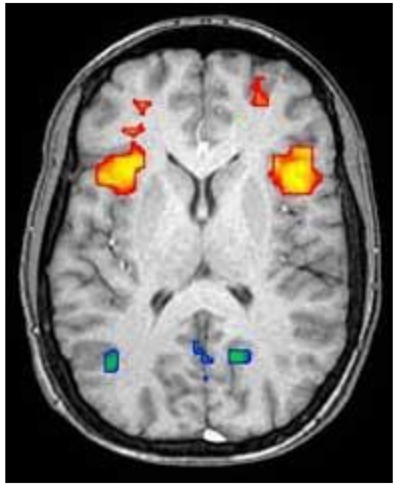


Perfusion

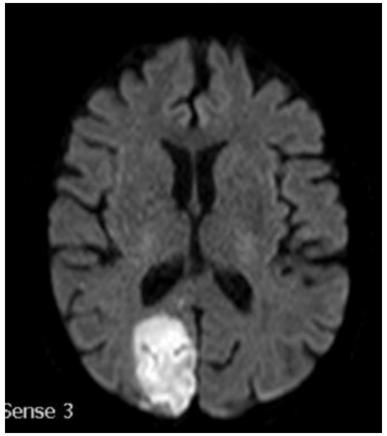


Biochemistry

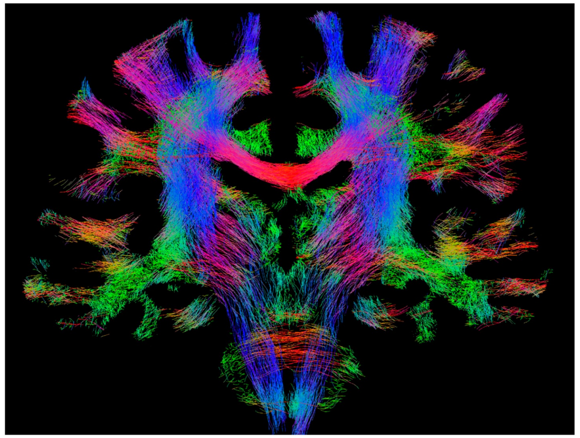




Neuronal activation

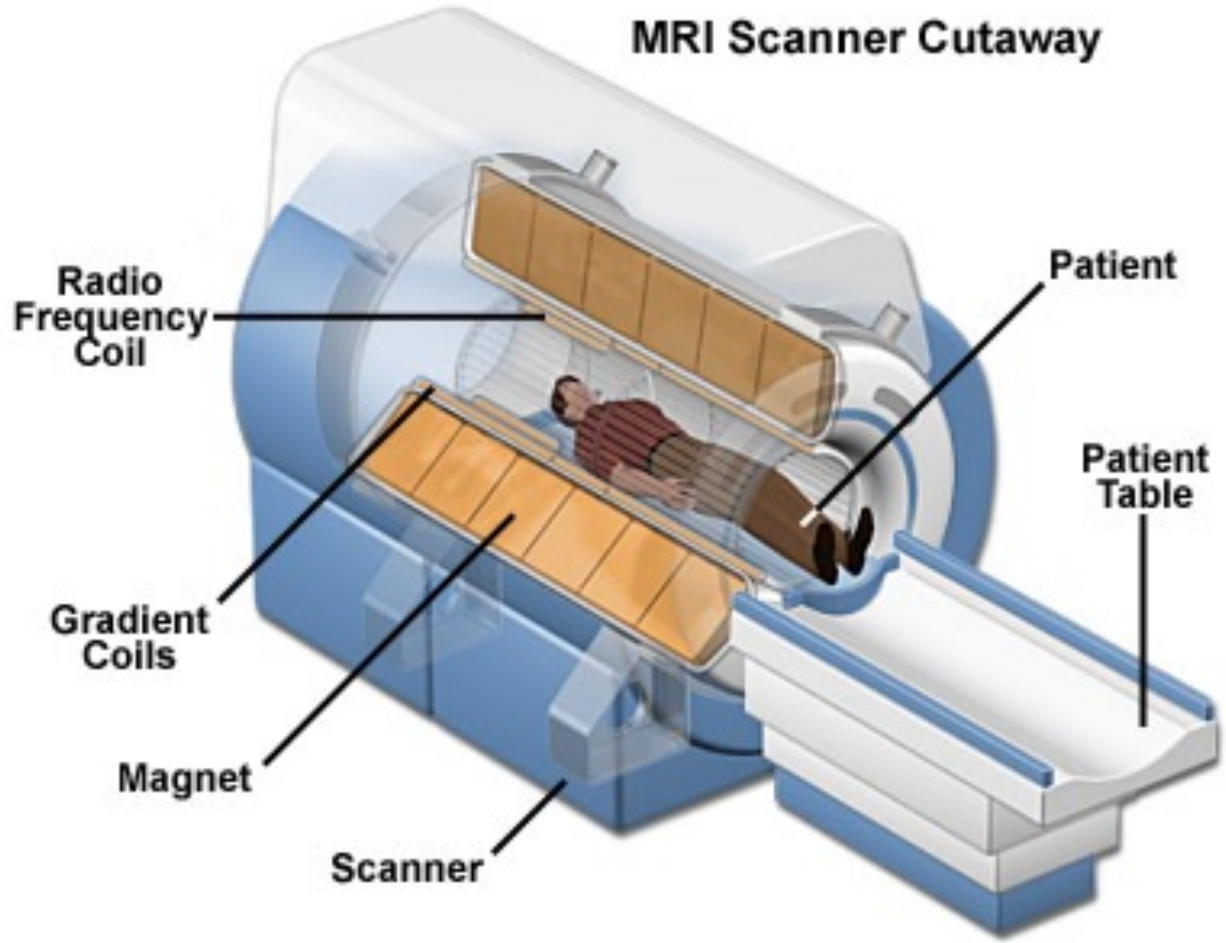


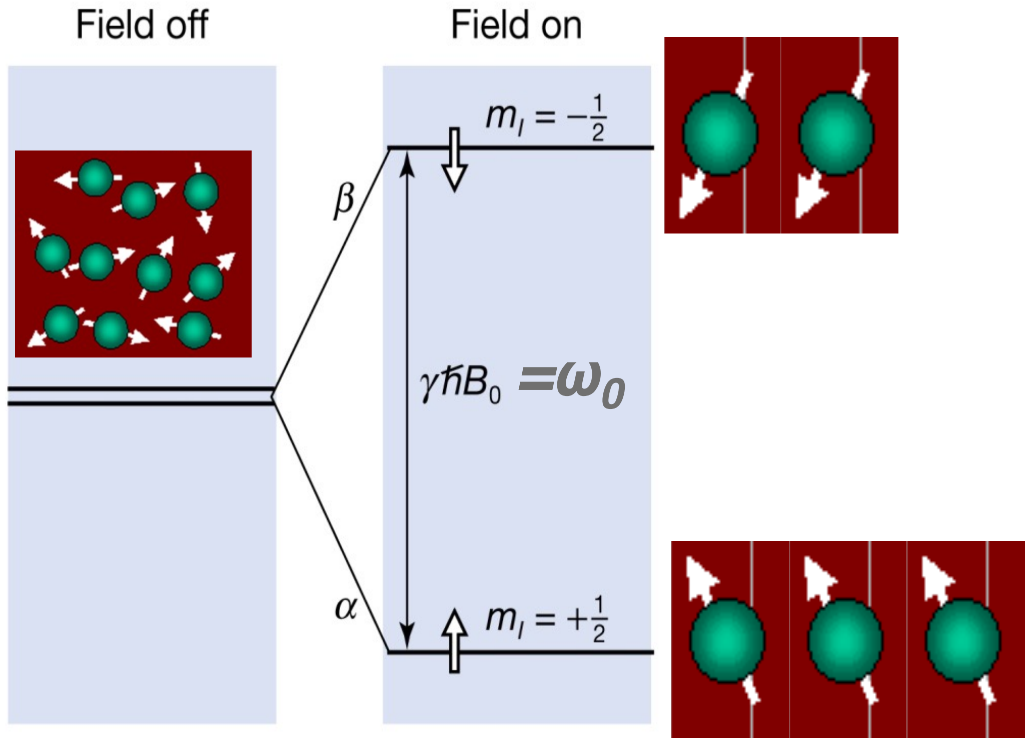
Water diffusion/microstructure



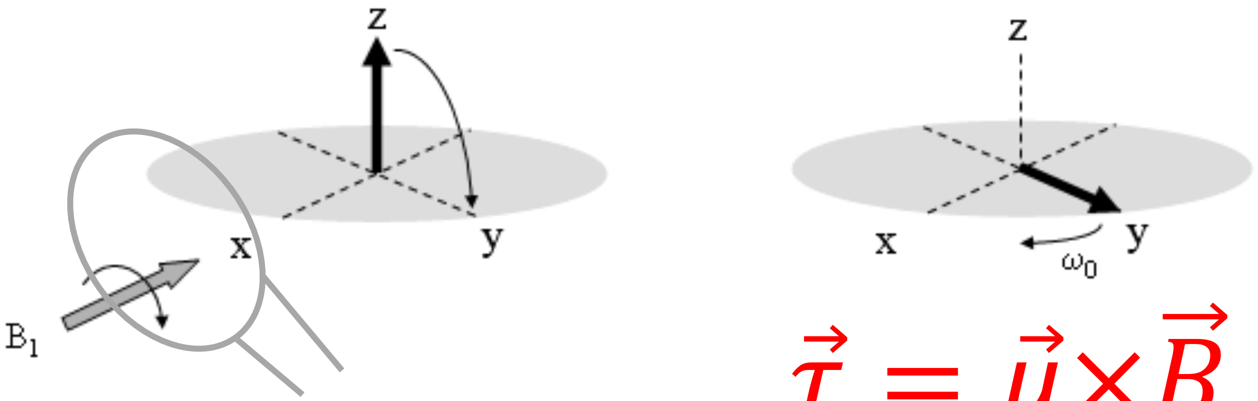
Structural connectivity

MRI


MRI Scanner Cutaway
Radio Frequency Coil
Patient
Patient Table
Gradient Coils
Magnet
Scanner


Field off
Field on
$m_I = -\frac{1}{2}$
β
$\gamma\hbar B_0 = \omega_0$
α
$m_I = +\frac{1}{2}$

Sum of all nuclear spins – the nuclear magnetization M

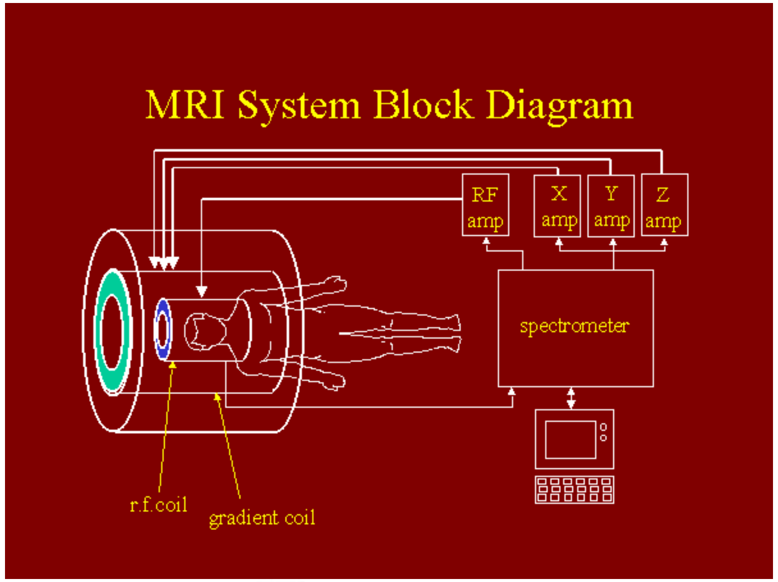


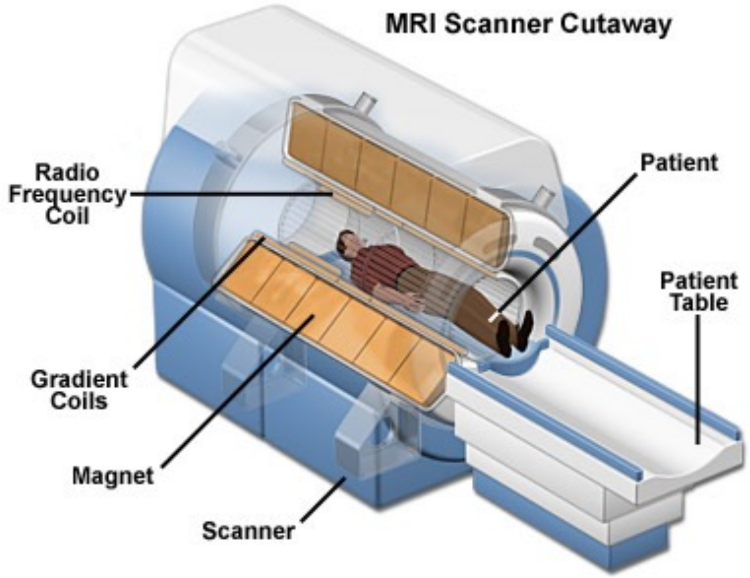
$$\vec{\tau} = \vec{\mu} \times \vec{B}$$

Ingredients for an MRI scanner

Basic ingredients and their function

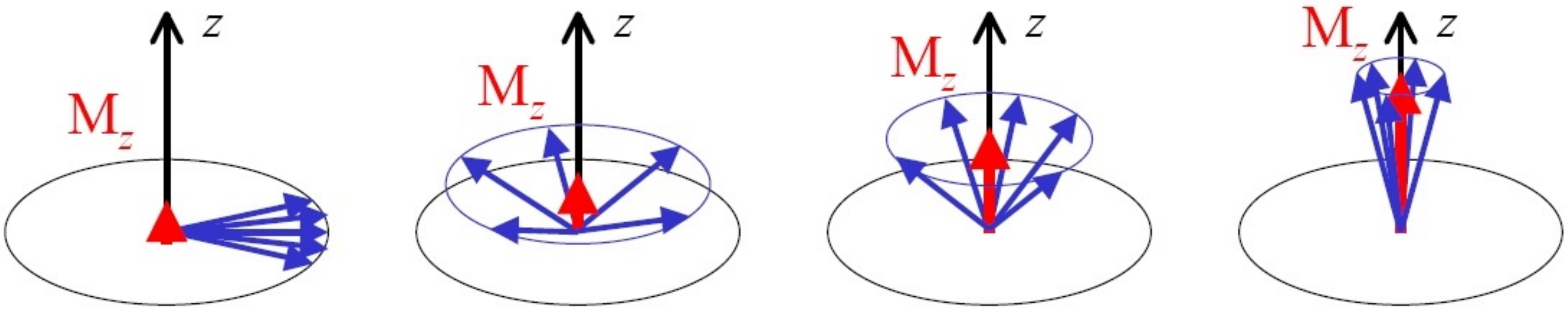
1. **Strong magnet**: creating strong *nuclear polarization* (**magnetization**);
2. **Radiofrequency (RF) coils**: **transmission of radiofrequency** and **reception of the signal** generated by the magnetization;
3. **Gradient coils**: **spatial encoding** signal in three directions (**creating an image**)



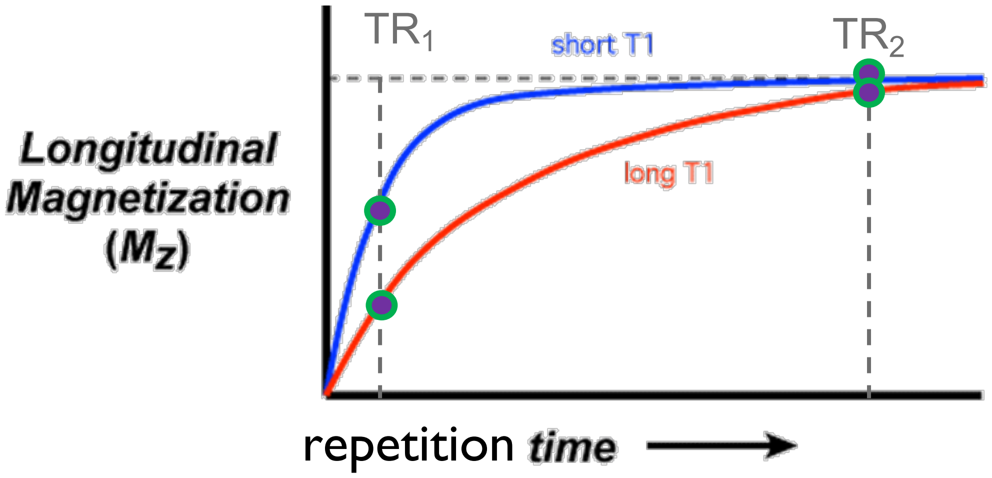


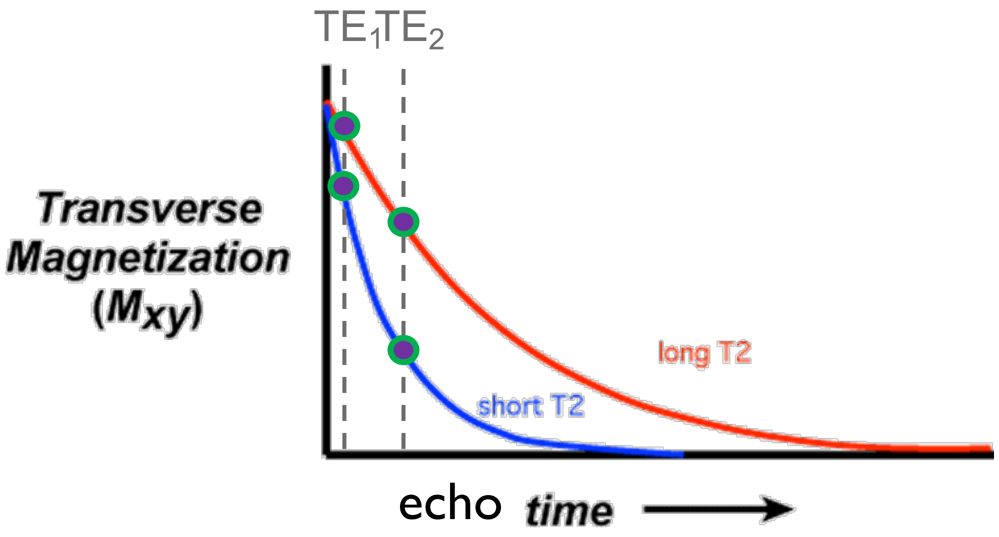
Relaxation: magnetization goes back to equilibrium

- The magnetization ***loses its coherence*** and ***returns to equilibrium*** :



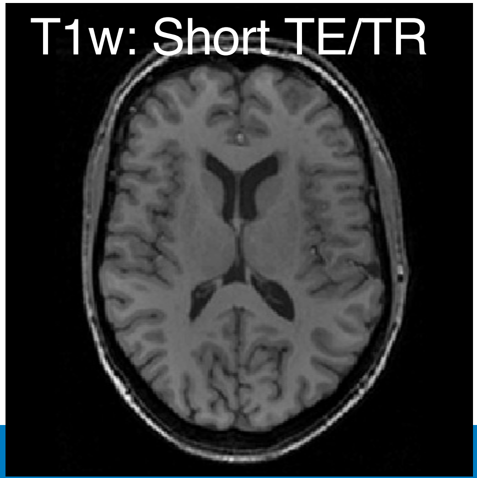
"Weighting" the signal according to relaxation times – the principle behind contrast in MRI

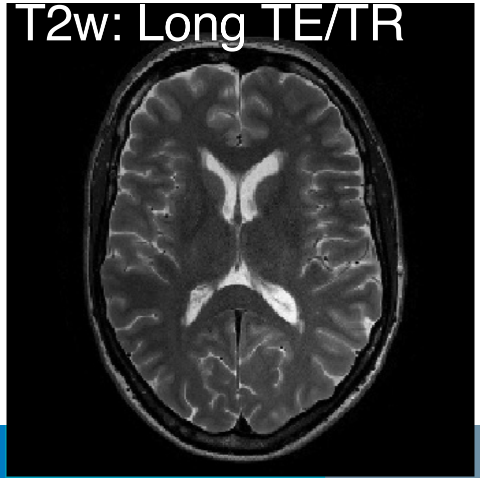




Tissue relaxation times (ms) at 3 Tesla

Tissue	T_1 (3T)	T_2 (3T)
Brain (white matter)	1100	60
Brain (gray matter)	1600	80
Liver	800	40
Skeletal muscle	1420	30
Lipid (subcutaneous)	360	130
Cartilage	1240	37

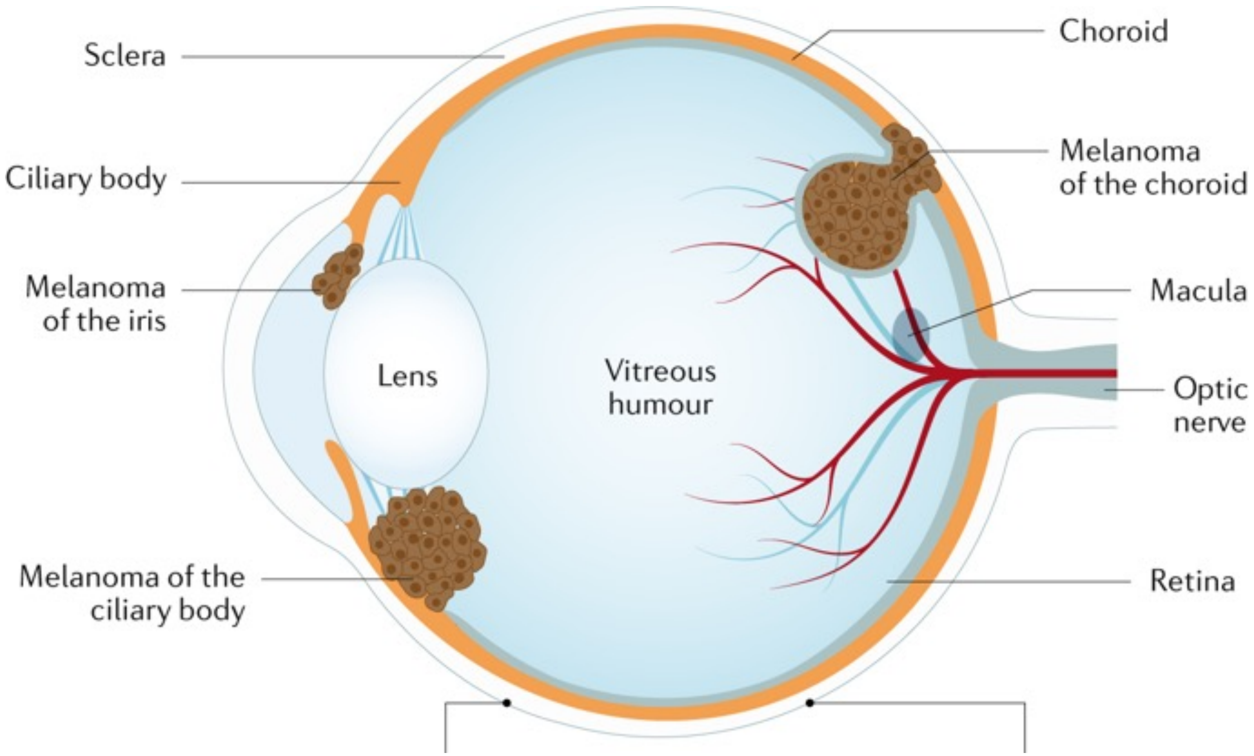




Oogtumoren

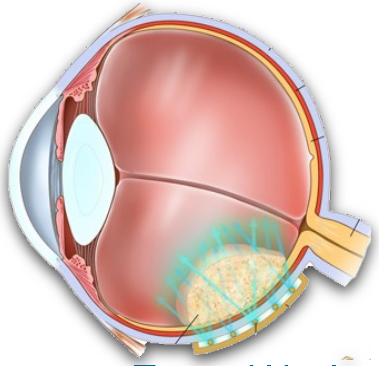
Uveal Melanoma

- Most common primary eye tumor
- Incidence: ±220 patients per year in NL
- Optimal treatment depends on size and location of tumor



Jager et al. Nat Rev Dis Primers (2020)

Brachytherapy
(<7mm thick)

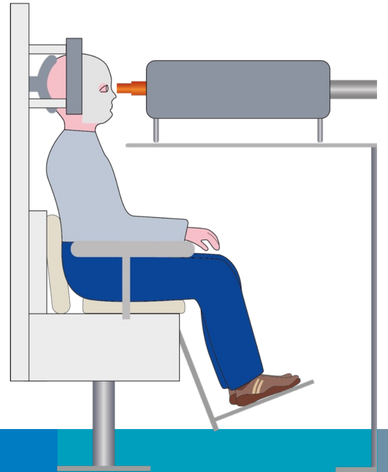


Terese Winslow LLC

Enucleation
(large tumors)

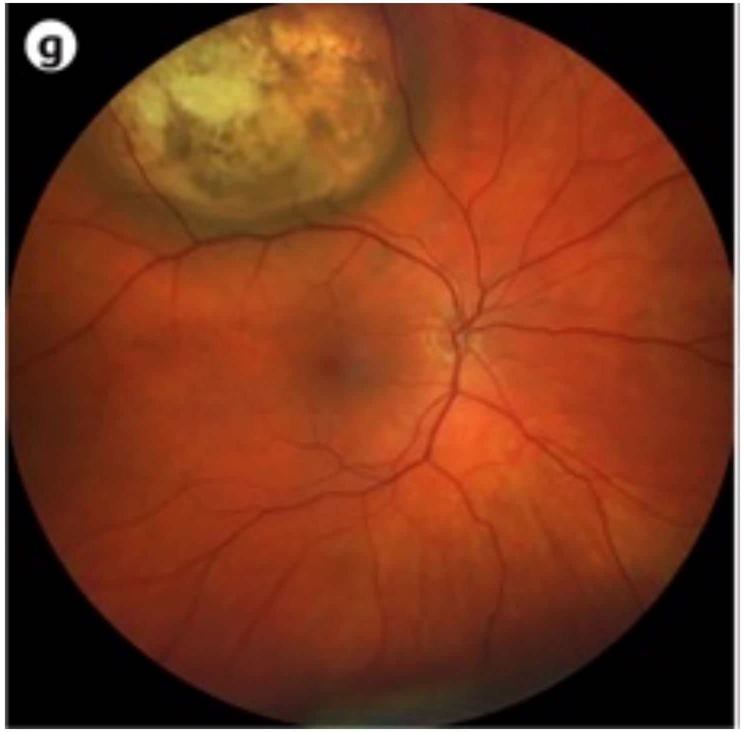
Corbis

Proton beam therapy

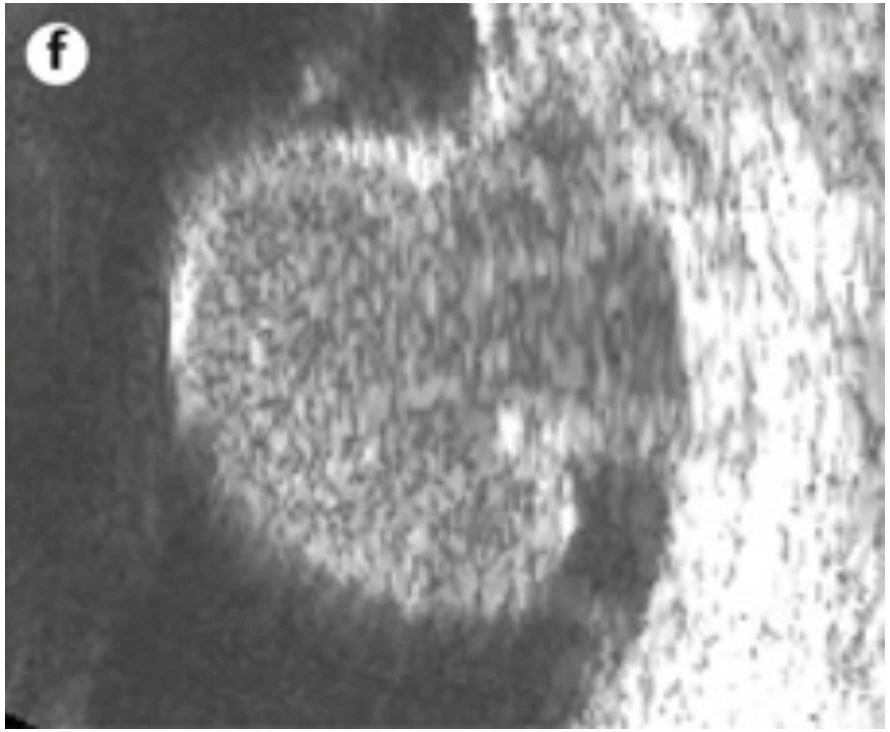


Conventional imaging modalities

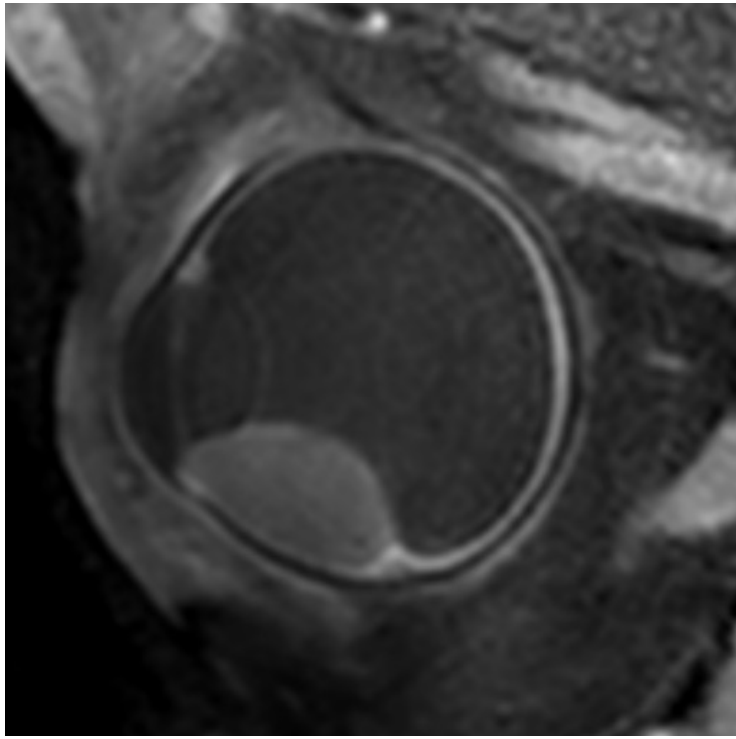
Fundus photography



2D Ultrasound



MRI

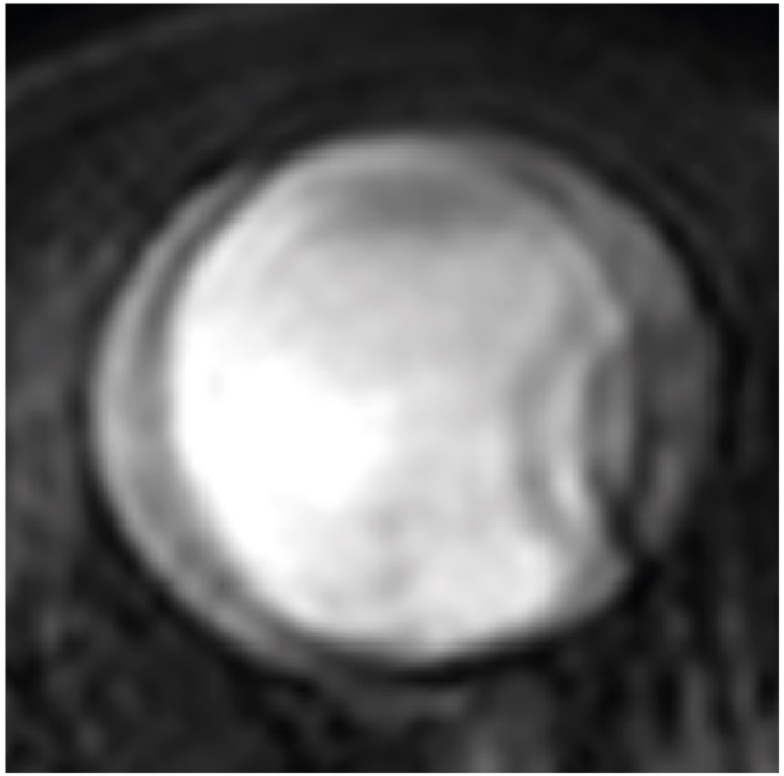


Jager et al. Nat Rev Dis Primers (2020)

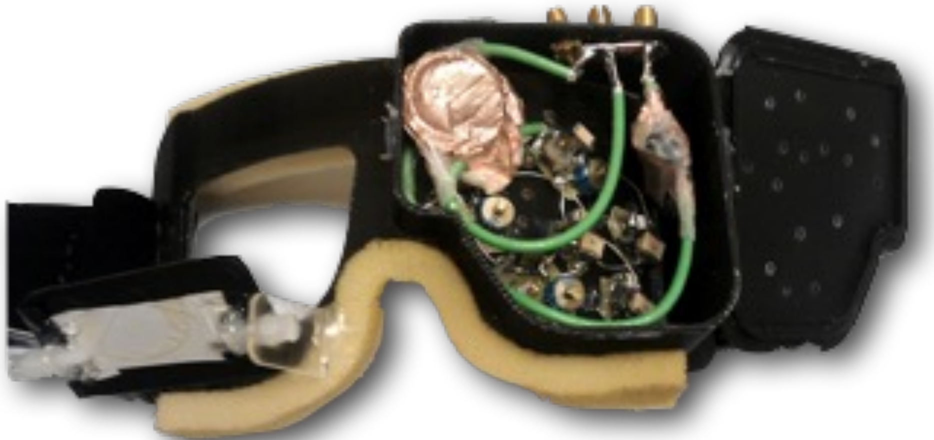
- Not the complete eye can be assessed optically
- No 3D visualization
- No biological information

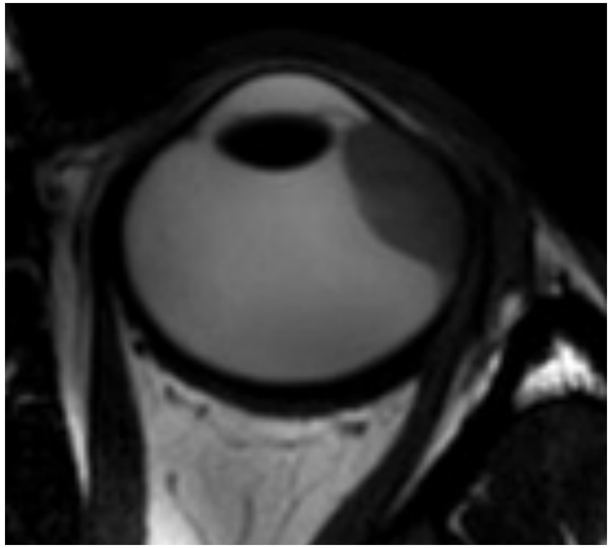
Ocular MRI is technically challenging

- The eye moves => motion artefacts render images undiagnositc
- The eye is small => high resolution result in long acquisition times
- Adjacent air/bony structures create additional (magnetic susceptiblity) artefacts

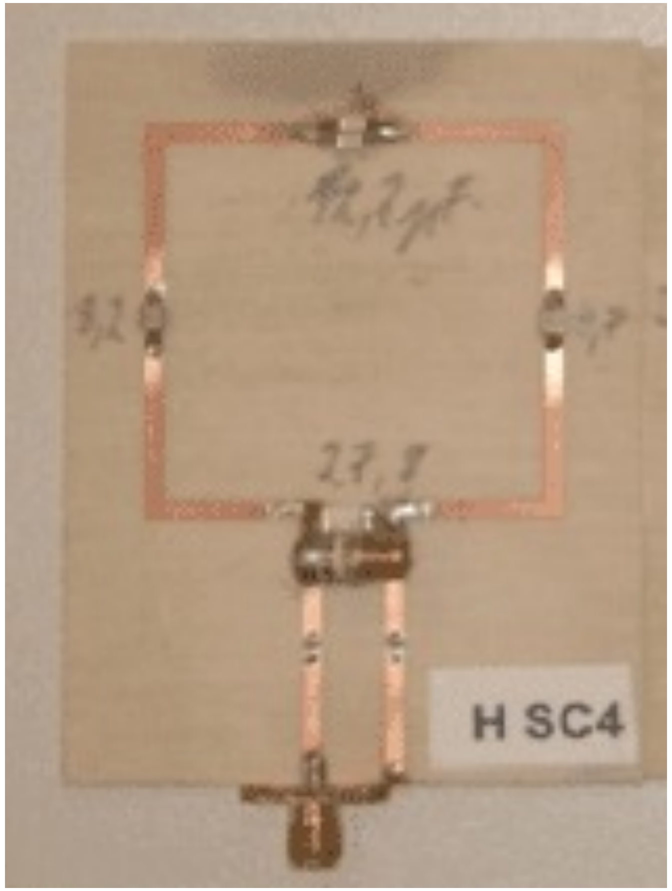


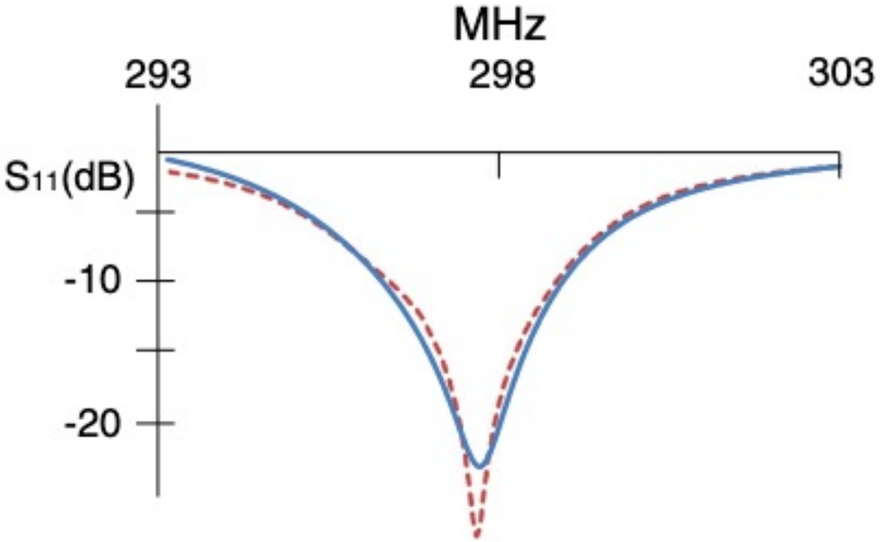
Van natuurkunde naar de zorg (en terug)

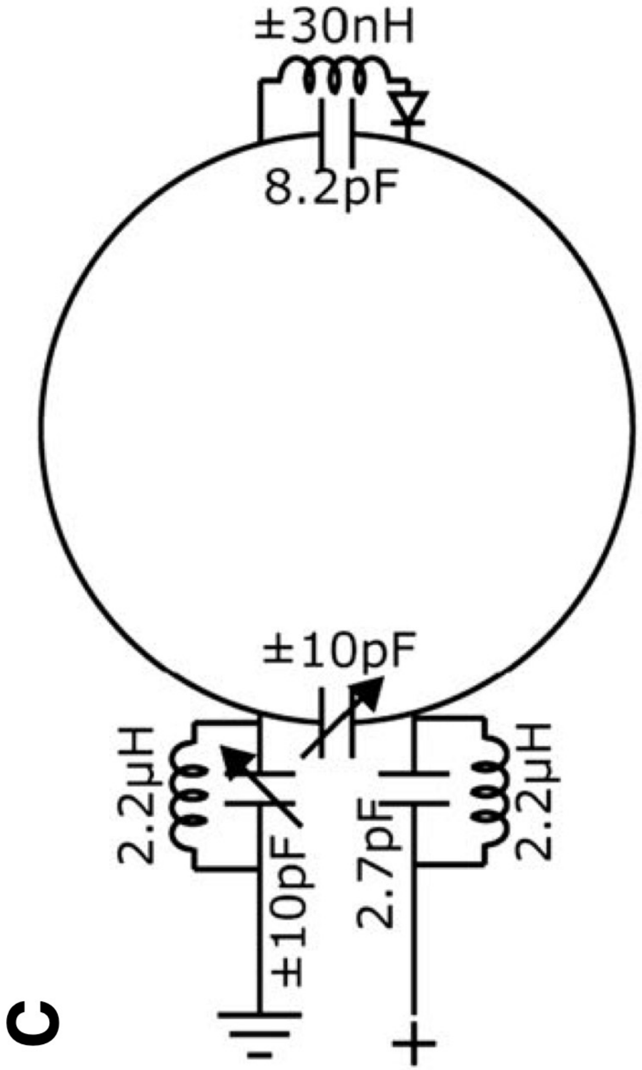




In house developed eye-coil

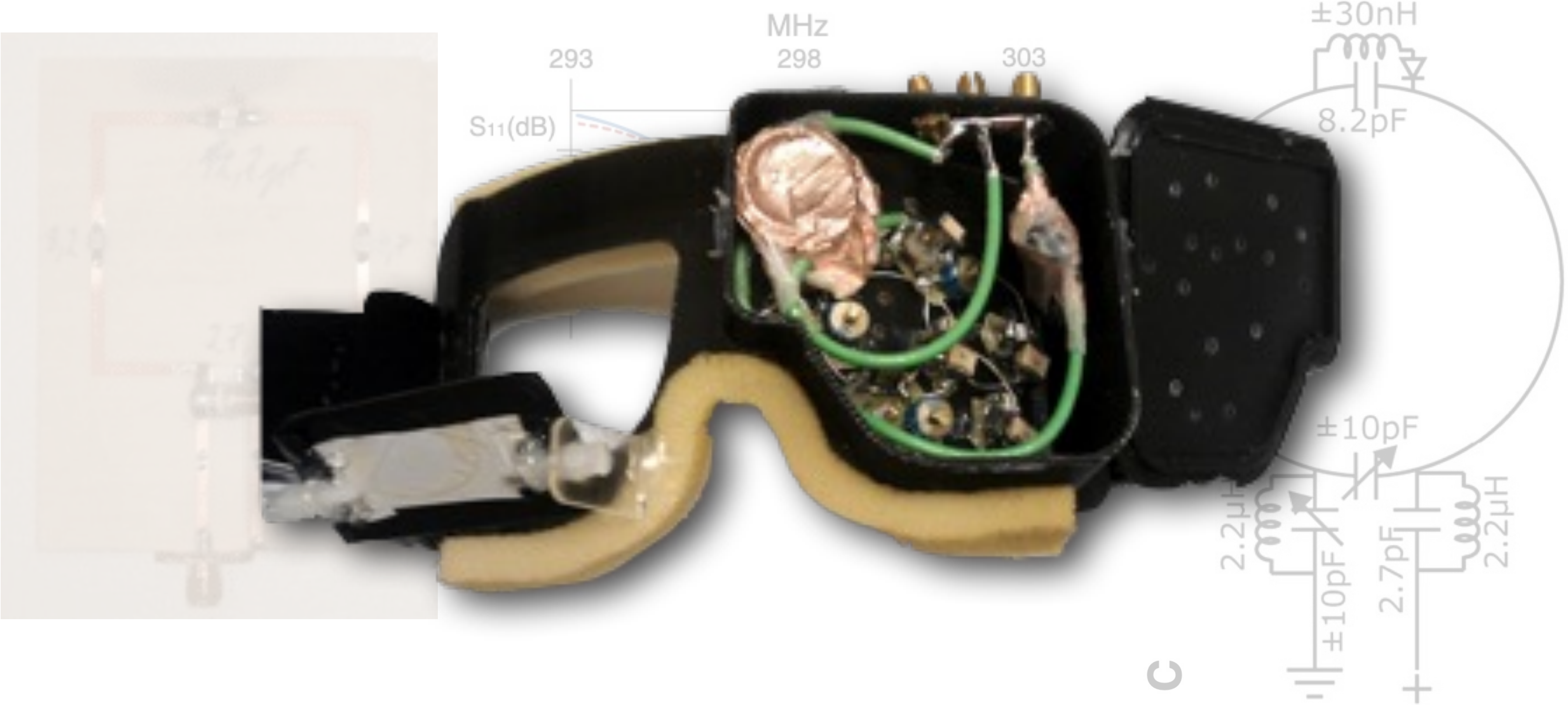






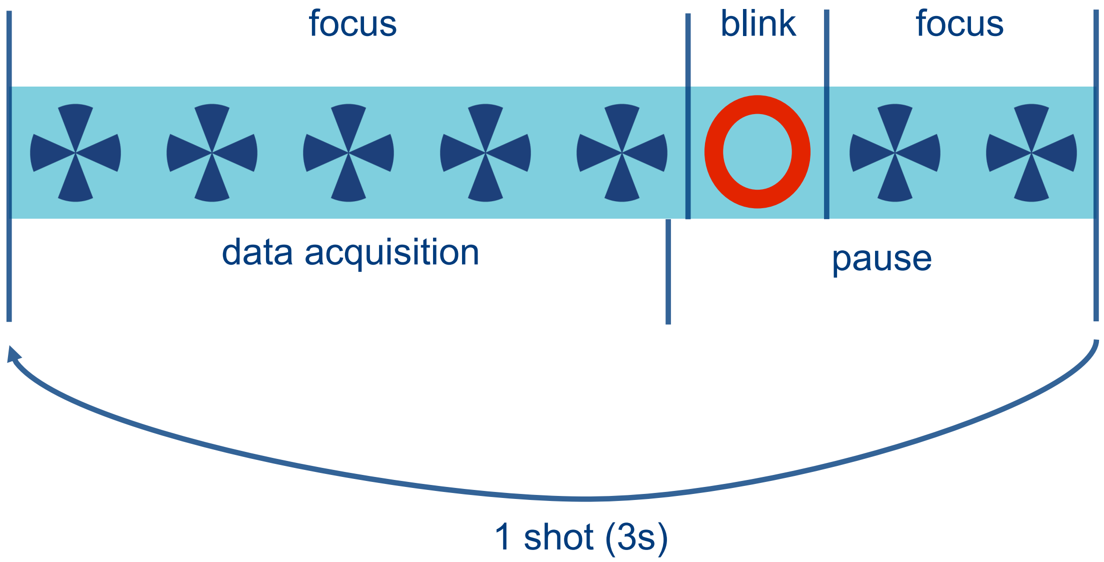
Beenakker et al, NMR in Biomed (2013)

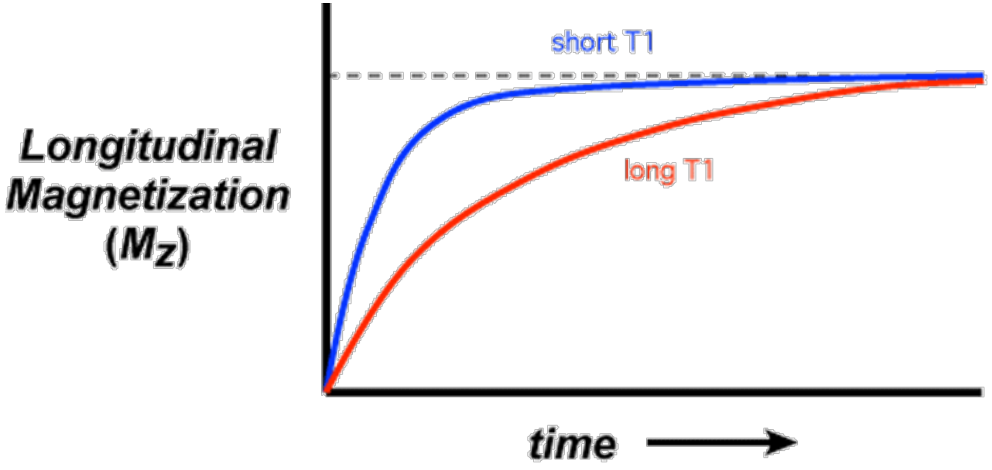
"Just" a simple LC-resonator



Beenakker et al, NMR in Biomed (2013)

Eye-motion





$$S = \left(M_0^* + (M_1 - M_0^*)e^{-\tau/2T1^*}\right)\sin\alpha \qquad (2)$$

where

$$T1^* = \left(\frac{1}{T1} - \frac{1}{TR}\ln(\cos\alpha)\right)^{-1}$$

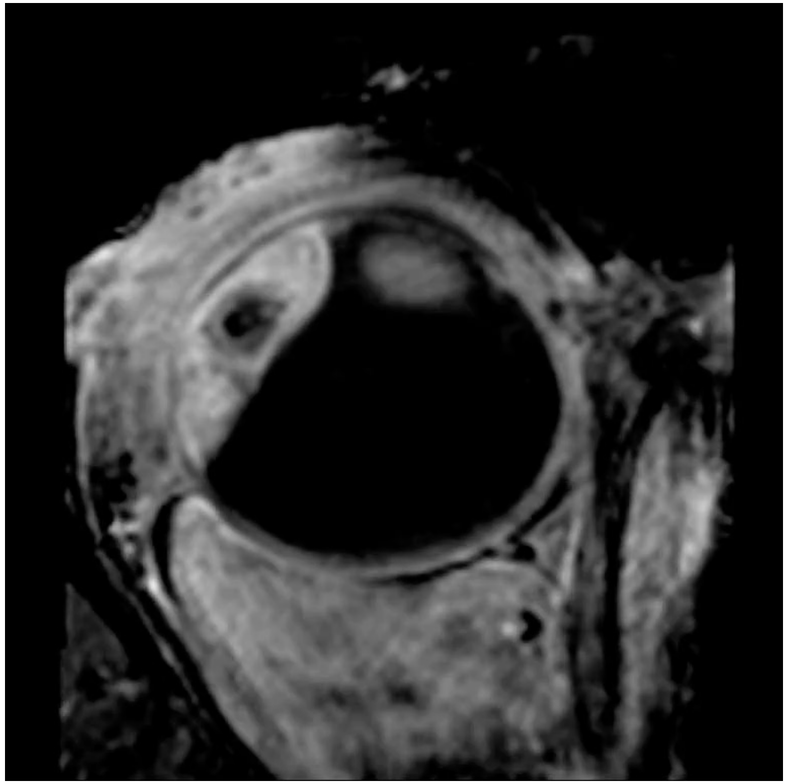
$$M_0^* = M_0\frac{1 - e^{-TR/T1}}{1 - e^{-TR/T1^*}} \qquad M_1 = \frac{A}{1 - B}$$

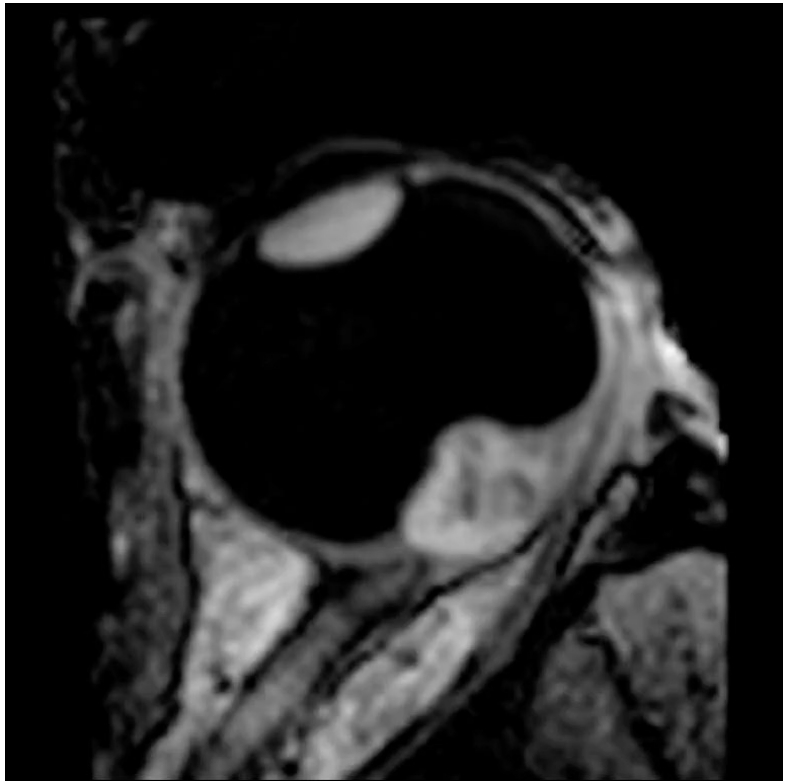
and

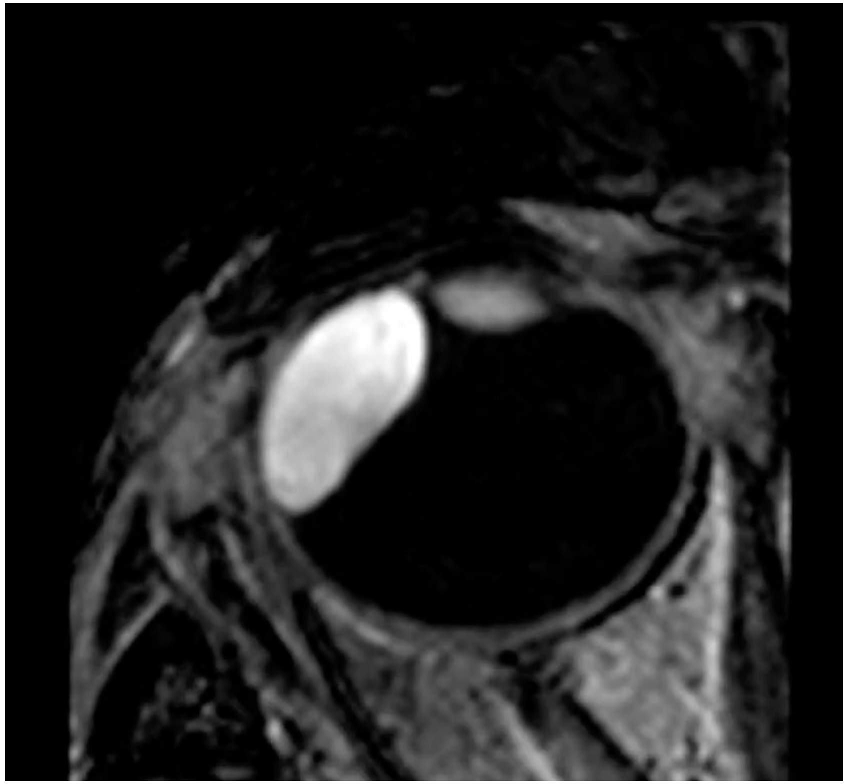
$$A = M_0(1 - e^{-TI/T1}) - \{M_0(1 - e^{-TD/T1})\}e^{-TI/T1}$$
$$- \{M_0^*(1 - e^{-\tau}/T1^*)\}e^{-TD/T1}e^{-TI/T1}$$
$$B = -e^{-\tau/T1^*}e^{-TD/T1}e^{-TI/T1} \qquad (3)$$

Beenakker et al, NMR in Biomed (2013)

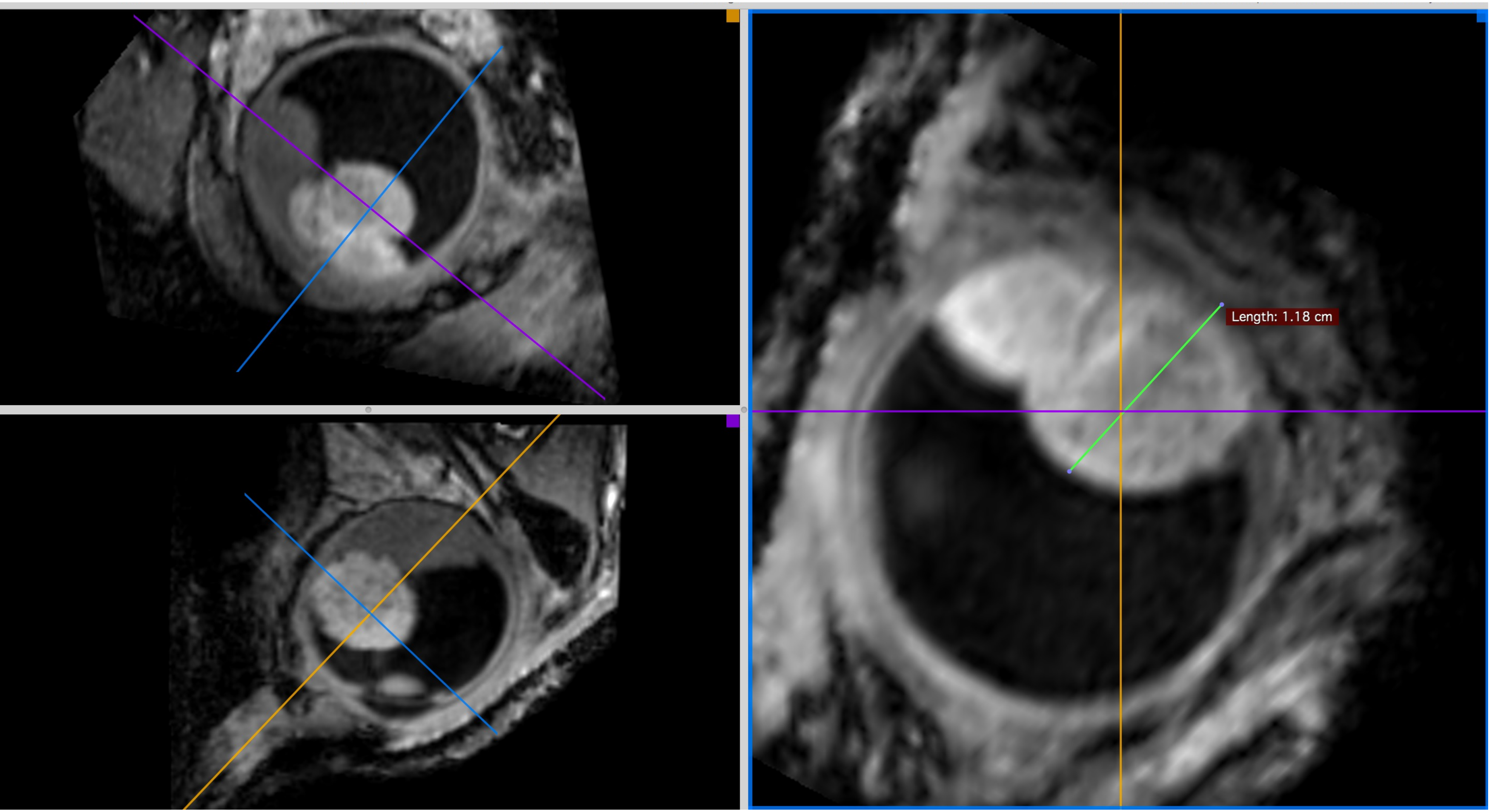
First images (2013)

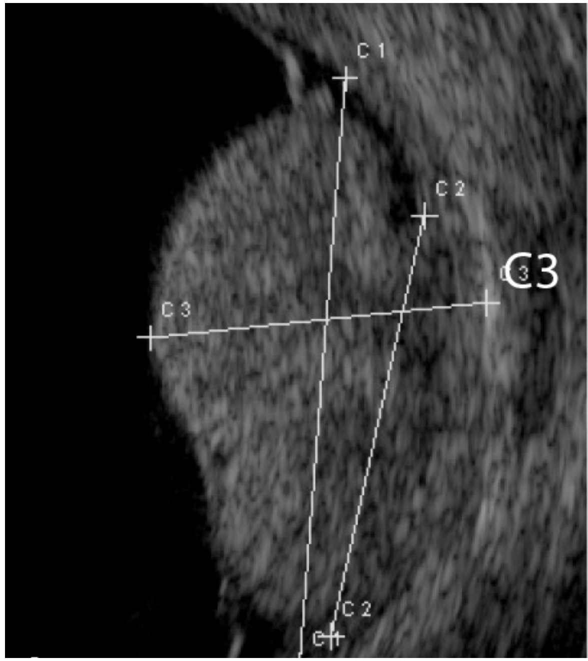




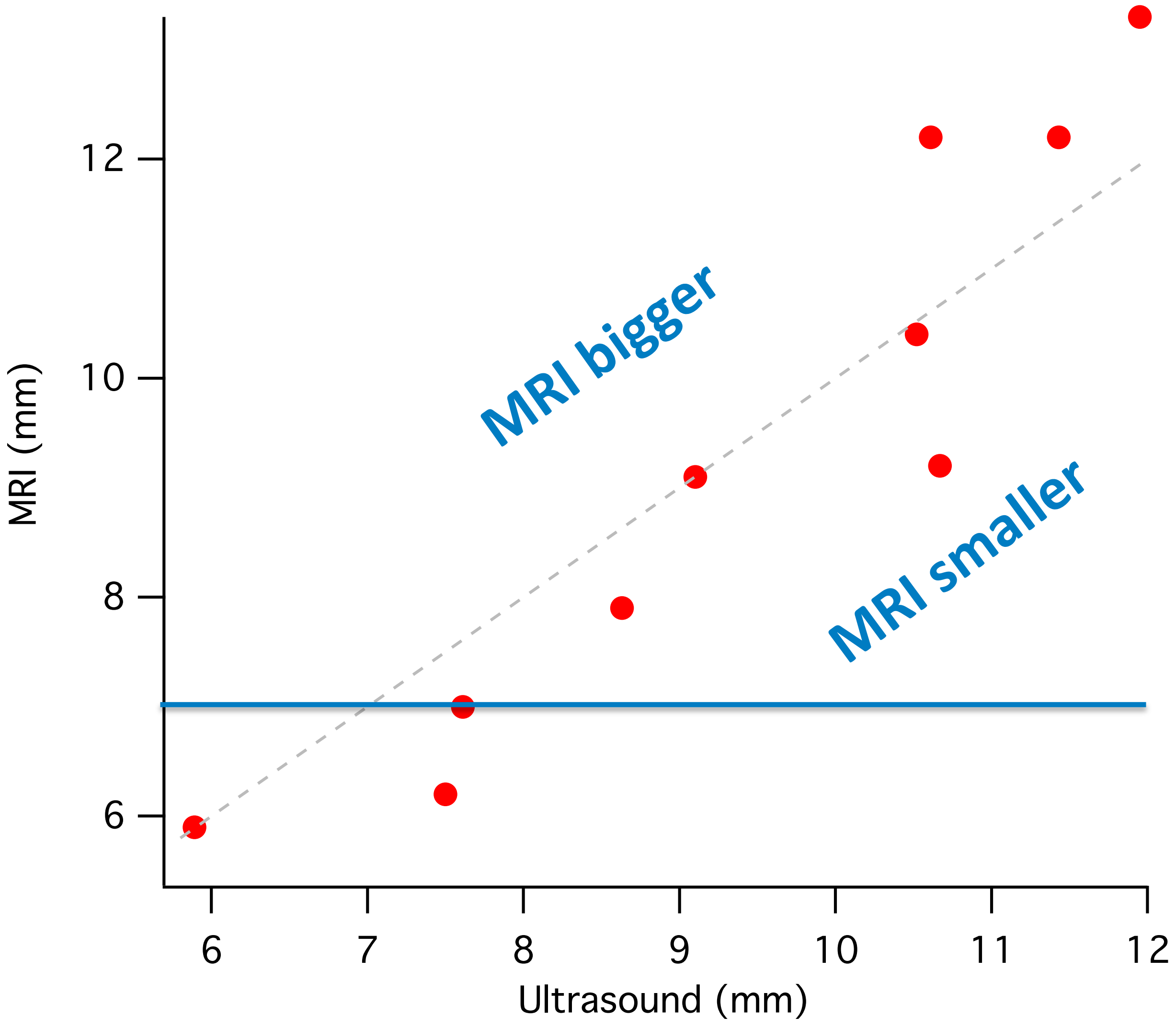


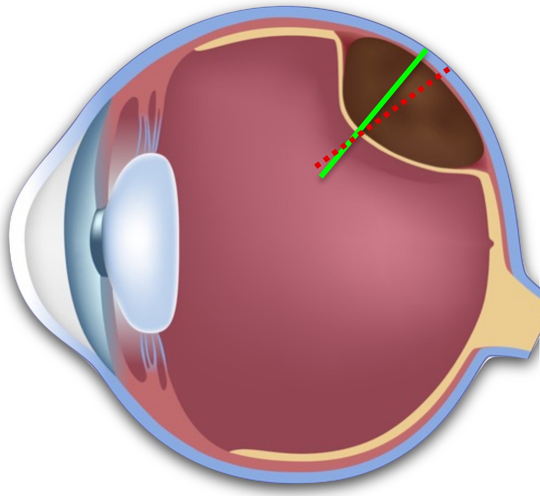
3D visualization intra-ocular tumor





Clinical impact





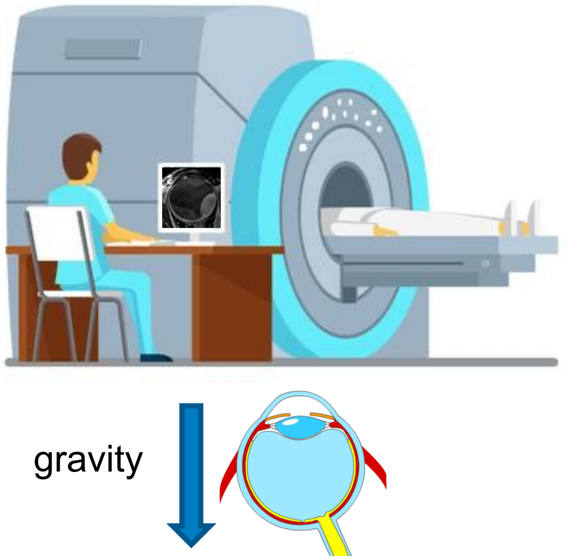
melanomanewstoday.com

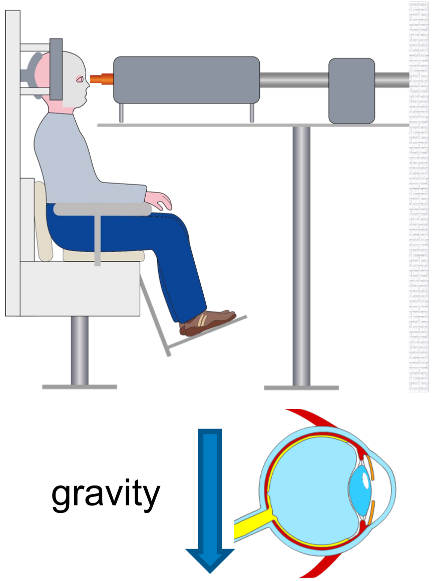
Enabled eye-preserving therapy in 2/10 patients!

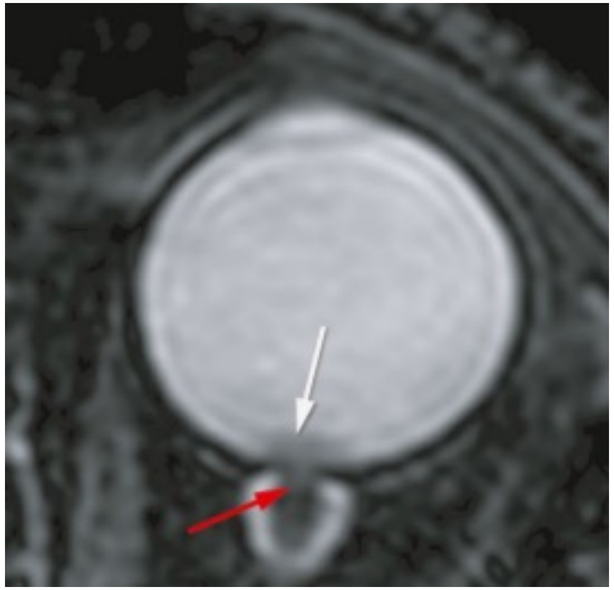
Beenakker et al, MAGMA (2016)

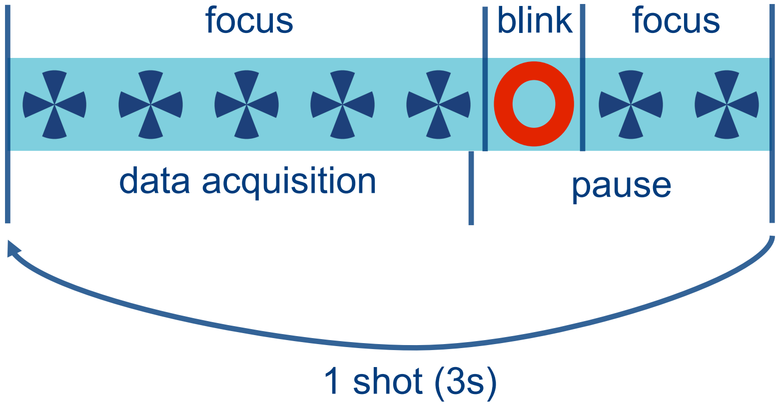
Multiple new questions

- Radiation oncologists: Should we change the required dose?
- Clinical phycics: Are your images geometrically accurate? Gravity effect?
- Radiologist: How certain are my observations?
- Technician: Cued-blinking doesn’t work for less coorperative patients
- Legal department: Research setup is not certified for clinical use

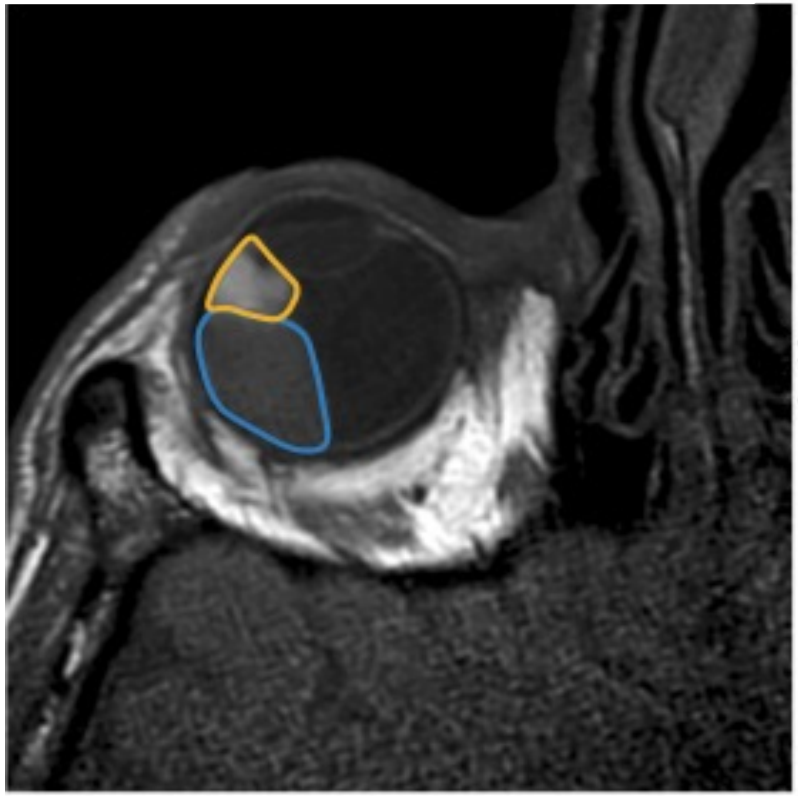








Validation of MRI findings and characteristics



Ferreira et al, MRI Characteristics of Uveal Melanoma with histopathological validation, Neuroradiology (2021)

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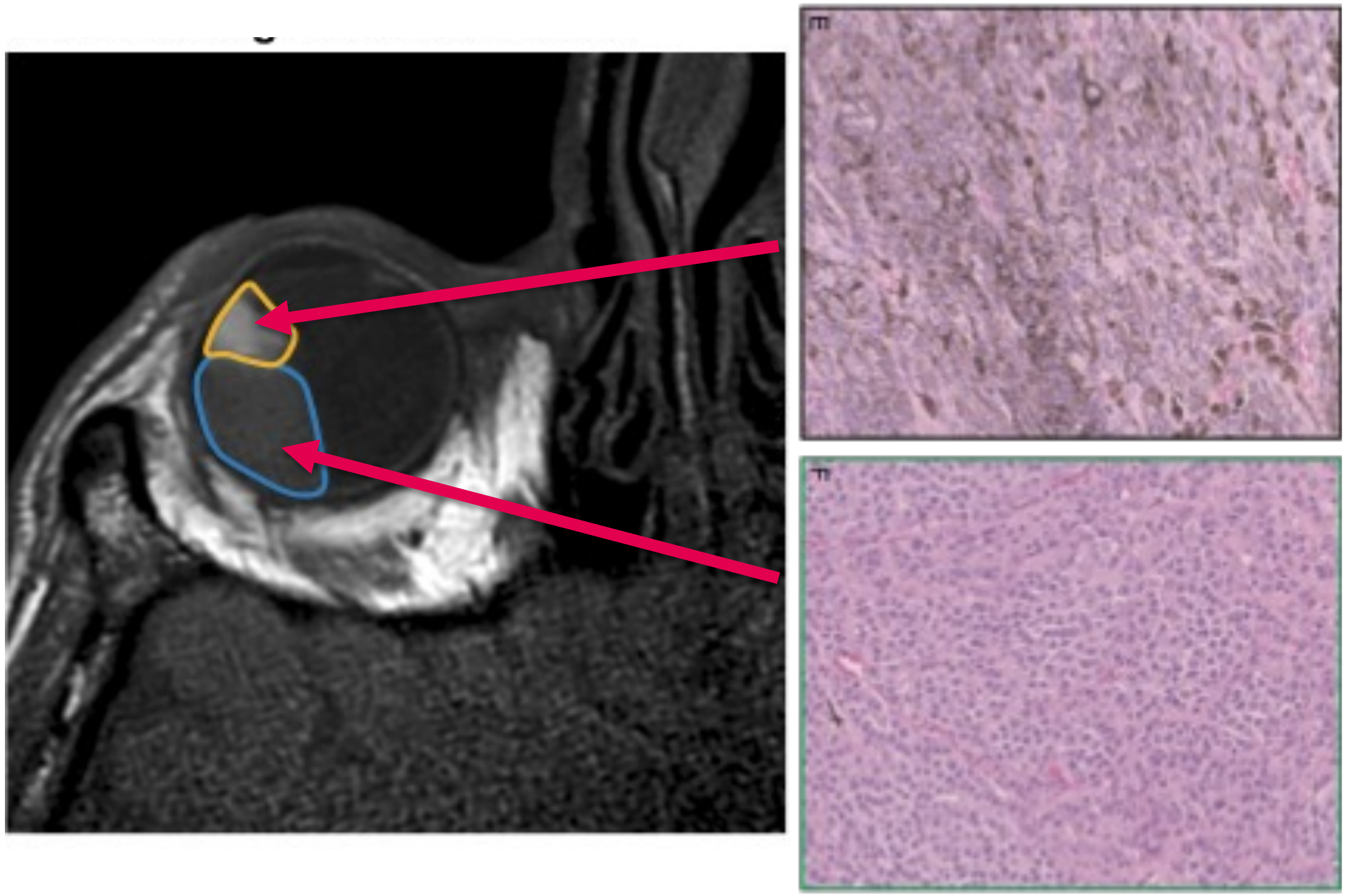

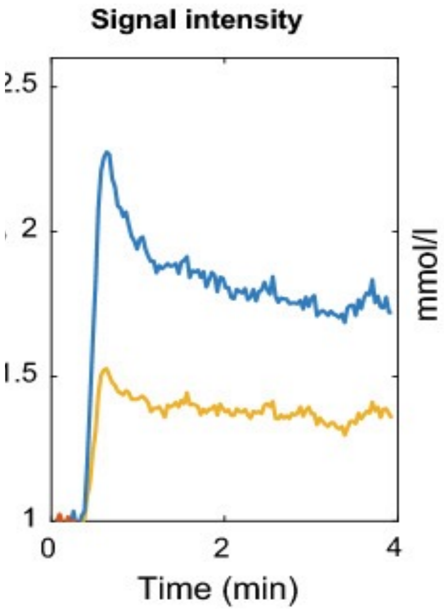

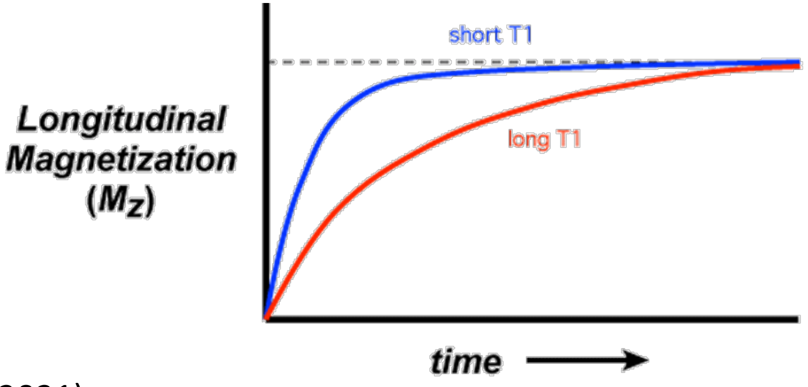

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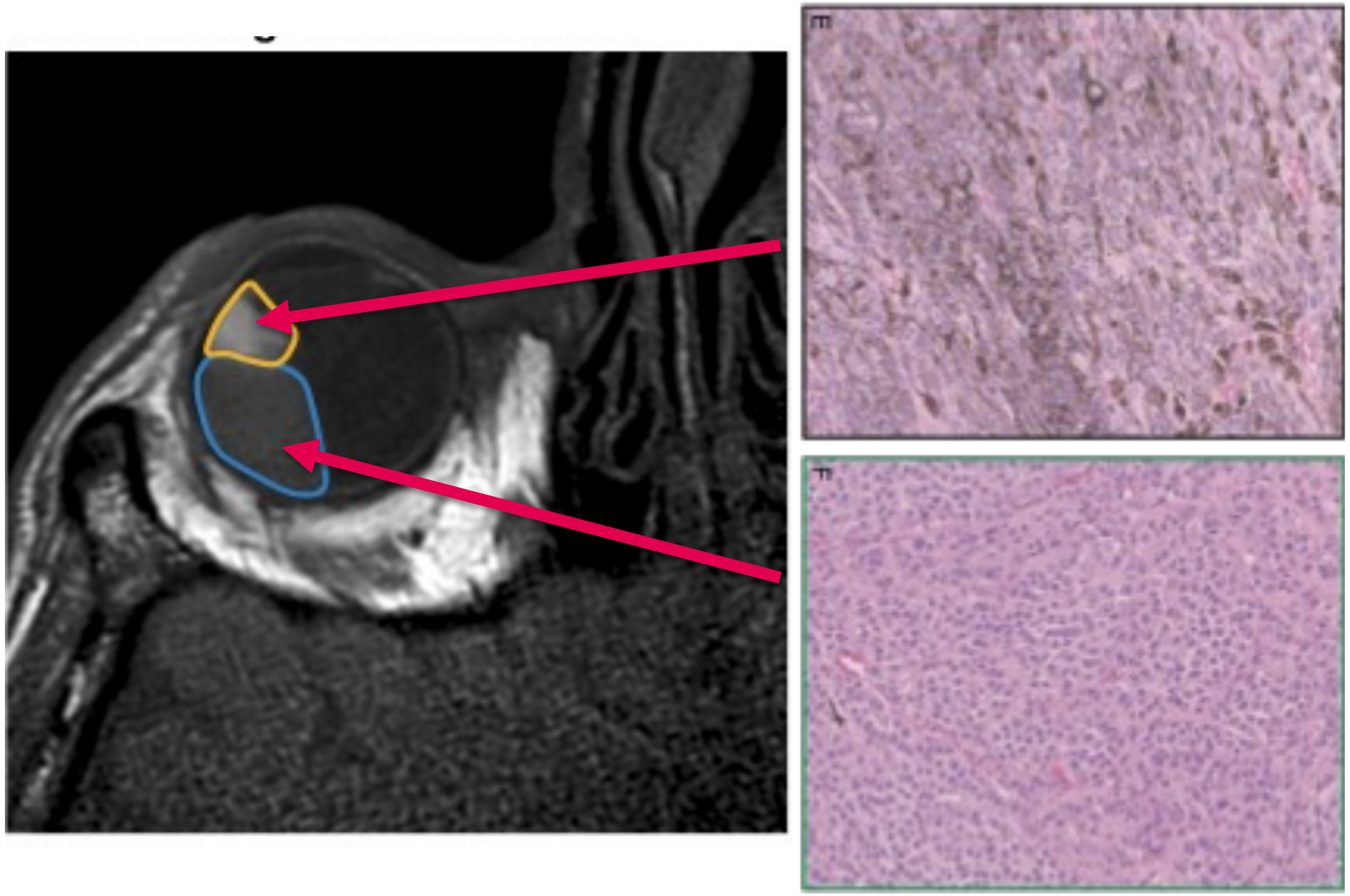

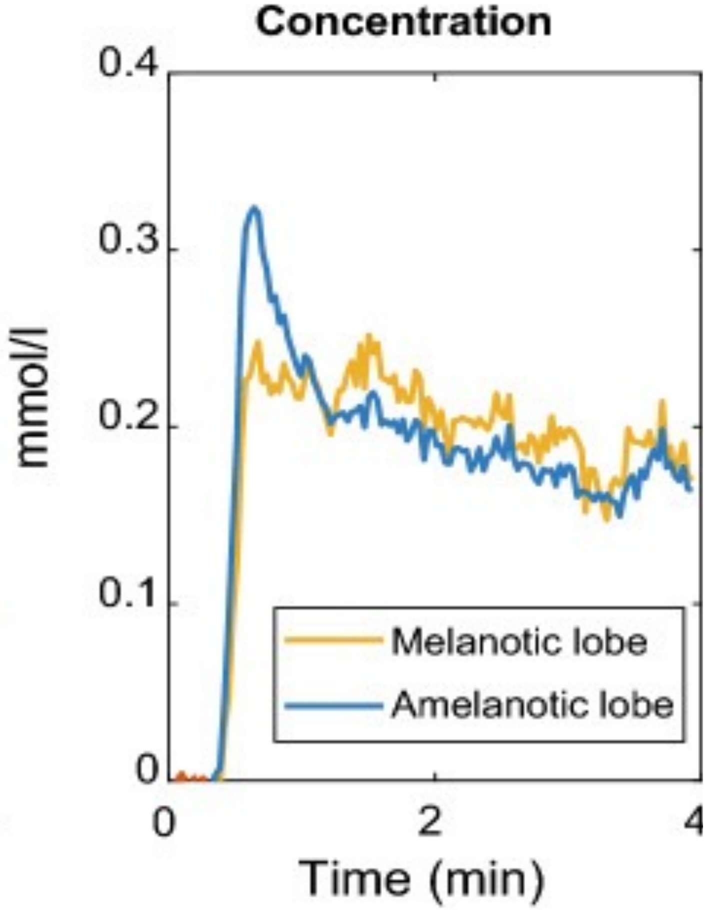

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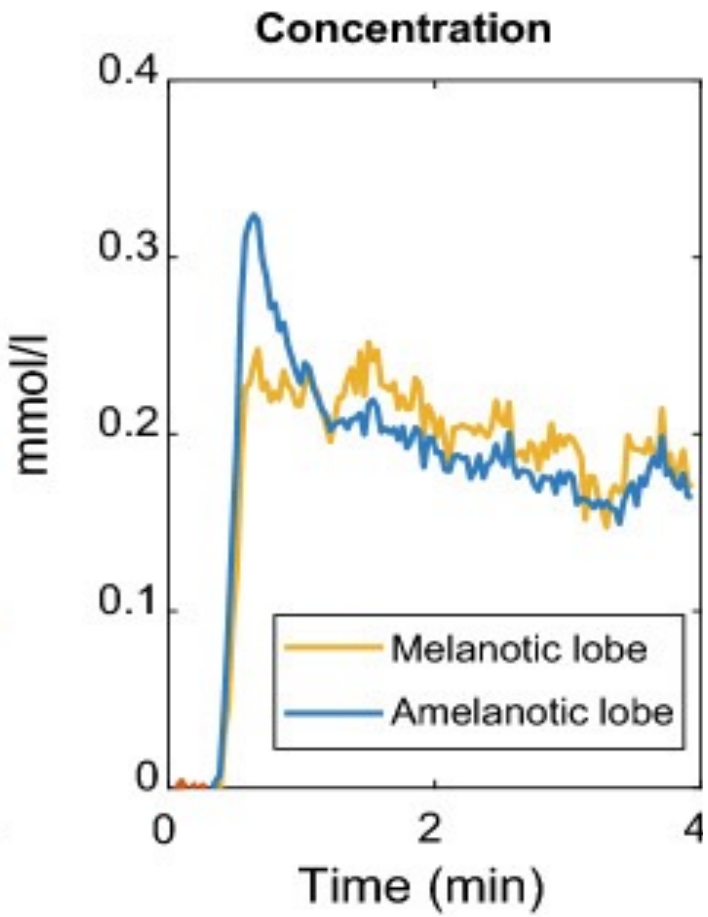
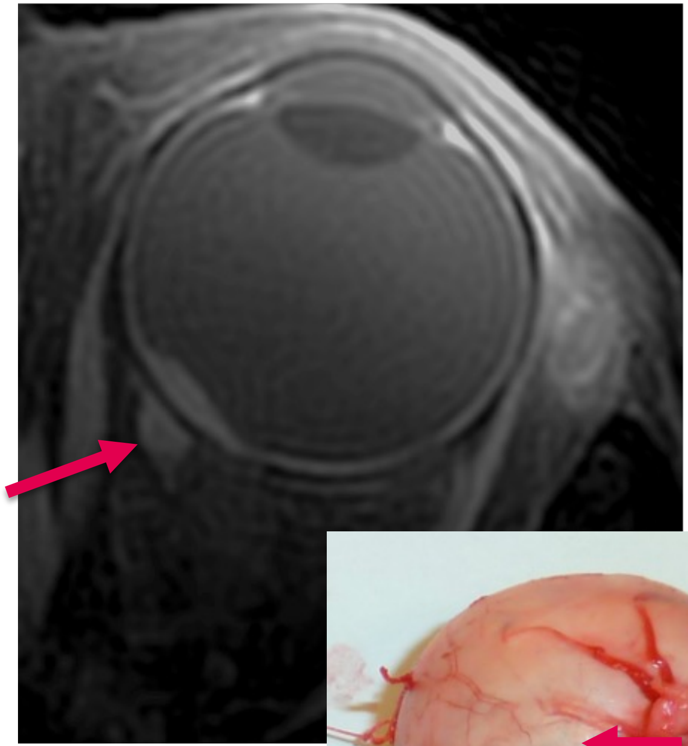


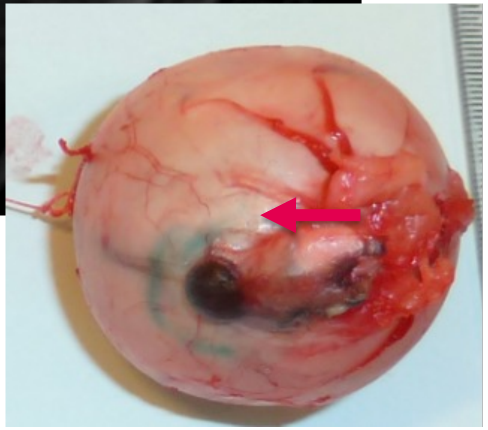
Evaluation of the error propagation

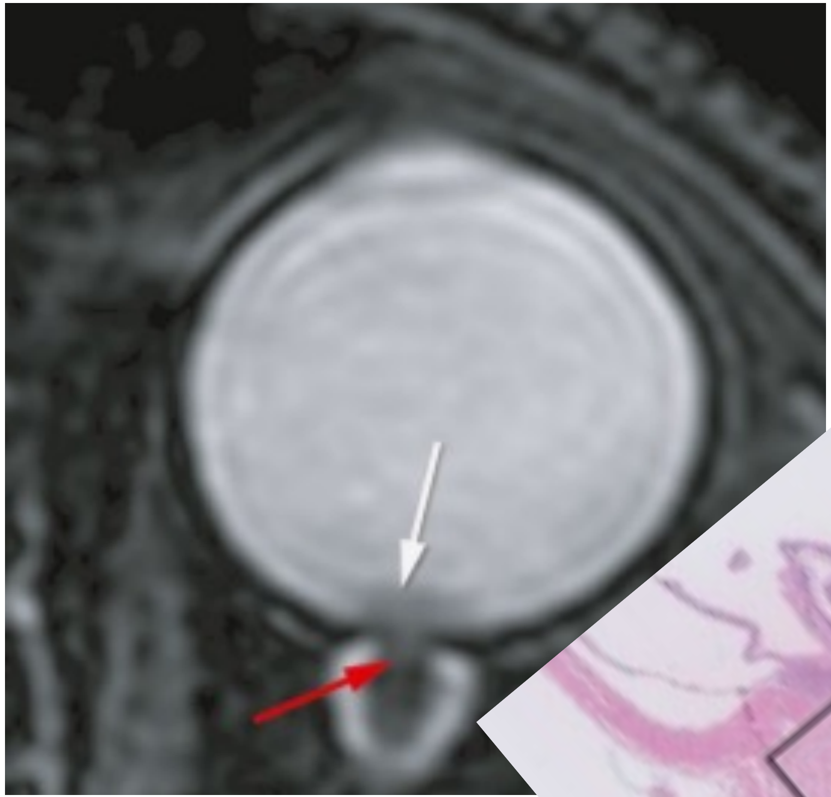
The effect of the precision error of the B_1^+, T_1 and registration on the pharmacokinetic were assessed. First, in two additional UM patients, the flip angle series and B_1^+ map were acquired twice to determine the repeatability of the B_1^+ and T_1 measurements. Second, the effect preci-

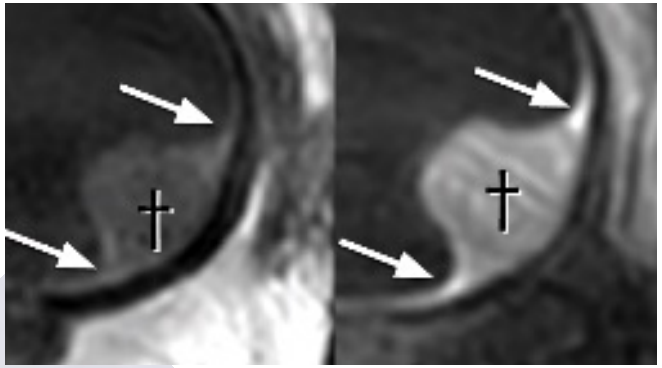
in B_1^+					
Relative change in	K^{trans}	v_e	K^{trans}	v_e	K^{trans}
Low achieved B_1 (82%)	− 10.7%	− 7.2%	− 3.6%	0.3%	6.4%
Normal achieved B_1(96%)	− 11.8%	− 7.4%	− 5.8%	− 1.2%	2.5%
Sensitivity to inaccuracies in T_1	T_1 − 60 ms		T_1 − 30 ms		T_1 + 30
Relative change	K^{trans}	v_e	K^{trans}	v_e	K^{trans}

Validation of MRI findings and characteristics



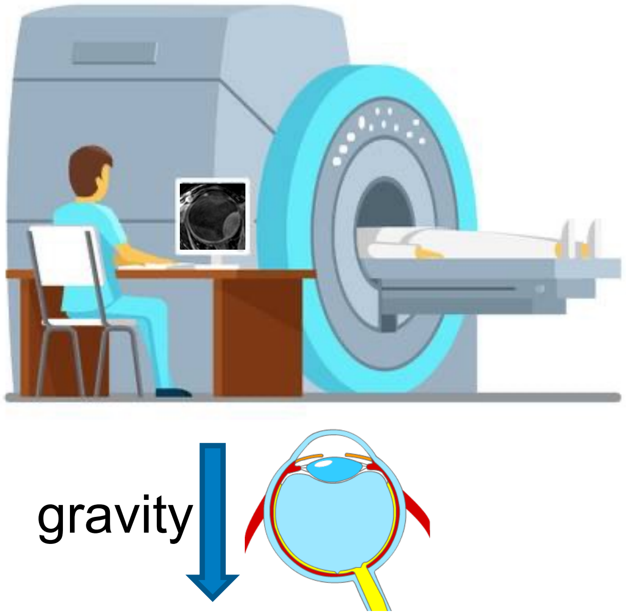


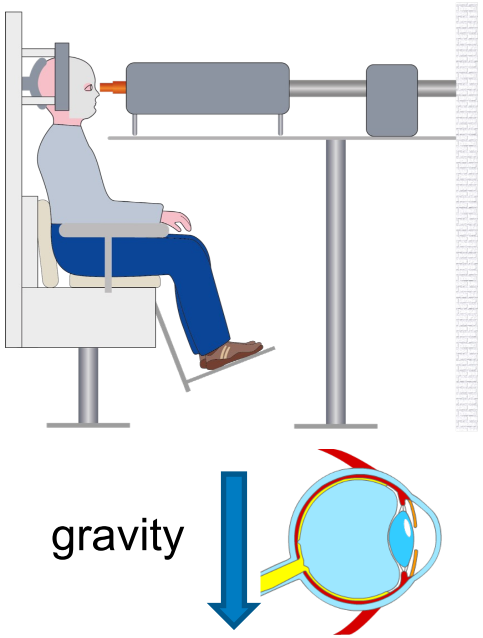




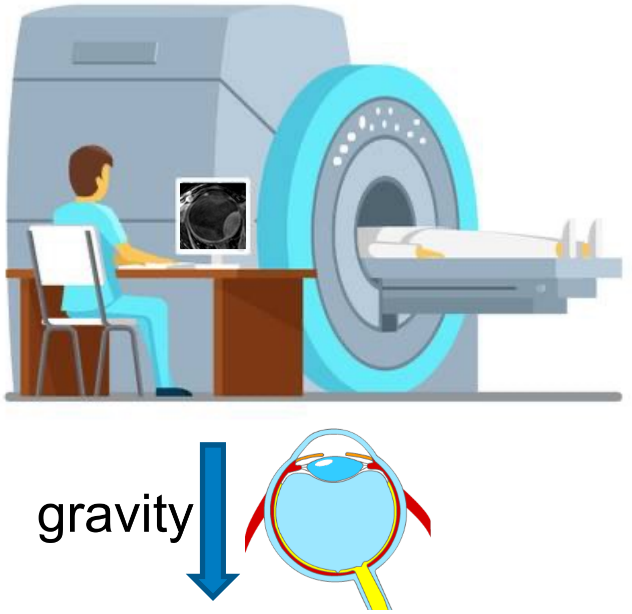
Ferreira et al, MRI Characteristics of Uveal Melanoma with histopathological validation, Neuroradiology (2021)

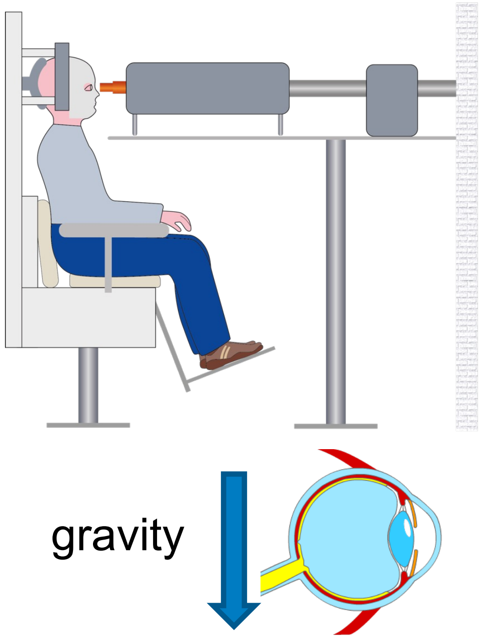
Supine vs sitting position

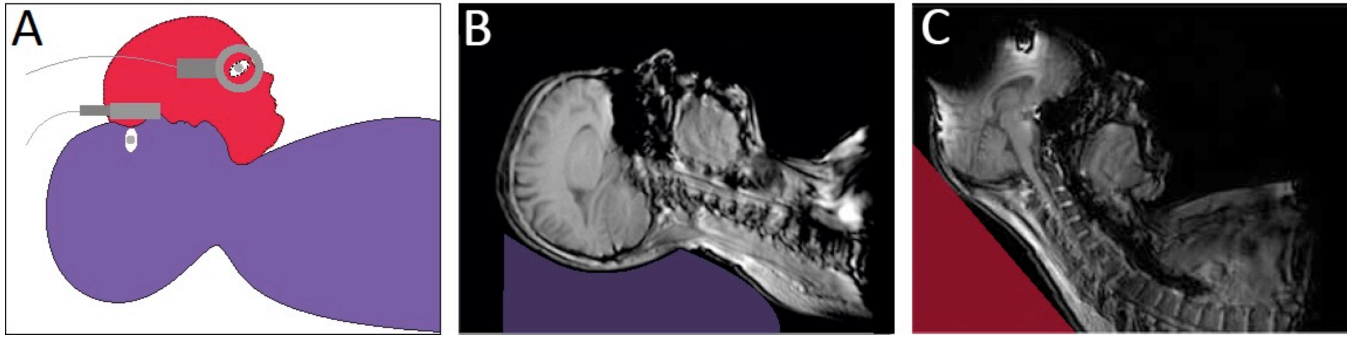


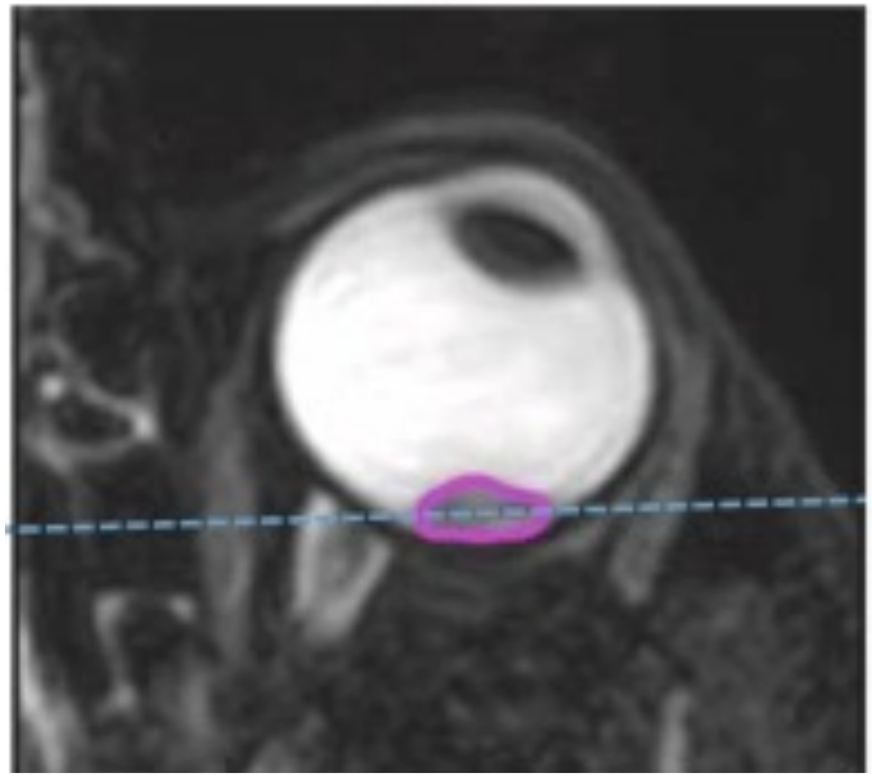


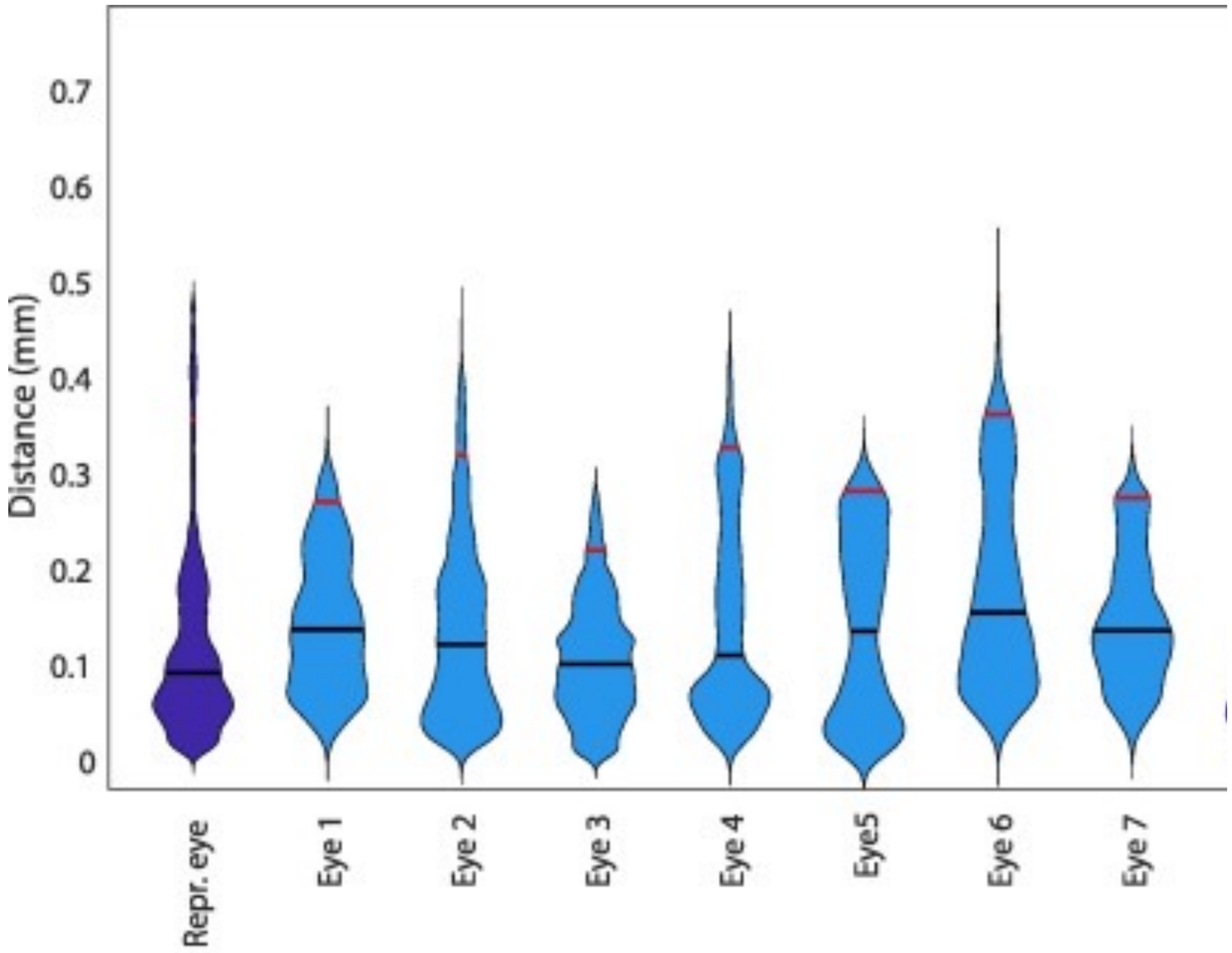
Supine vs sitting position



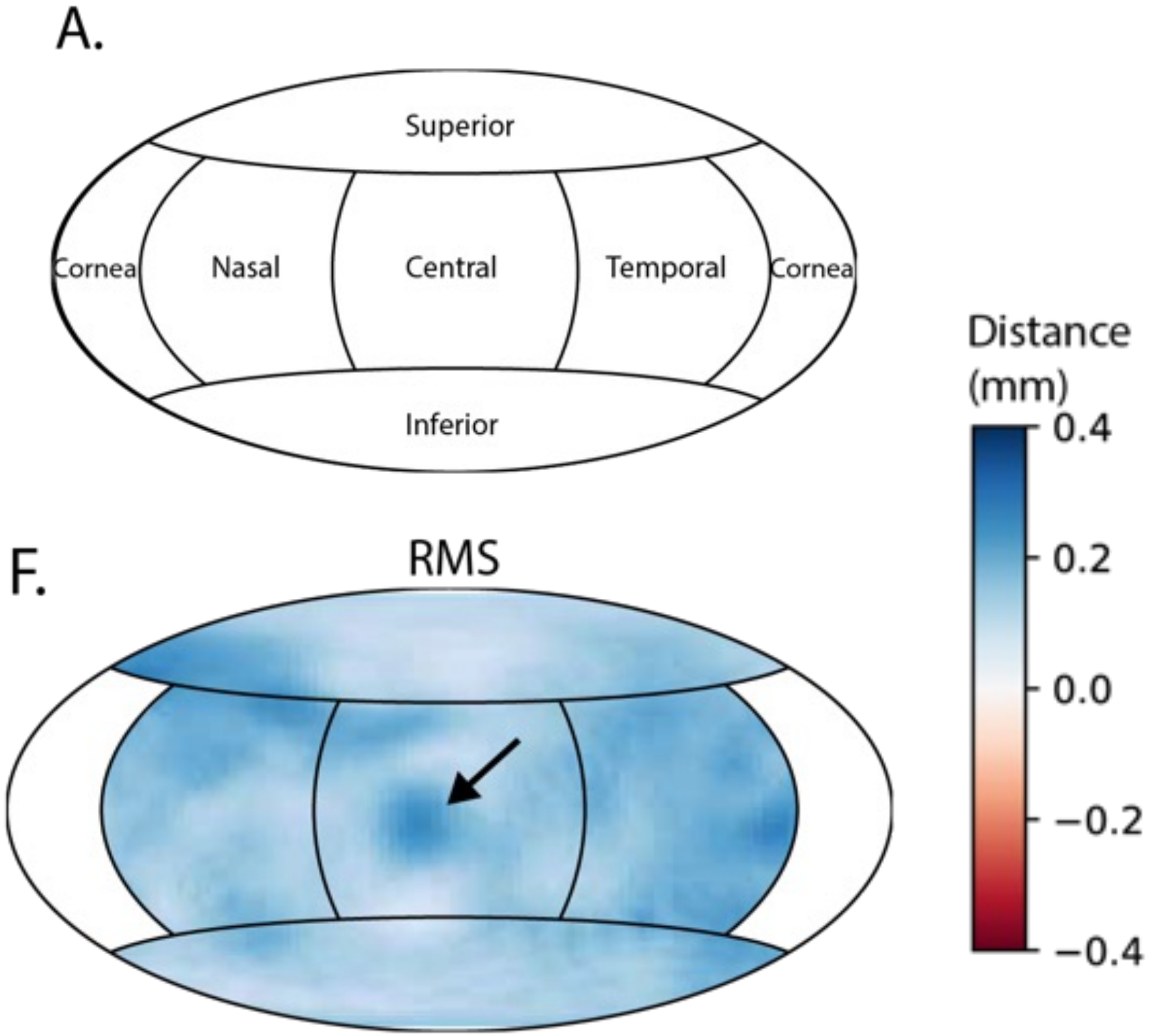








Distance (mm)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Repr. eye
Eye 1
Eye 2
Eye 3
Eye 4
Eye5
Eye 6
Eye 7

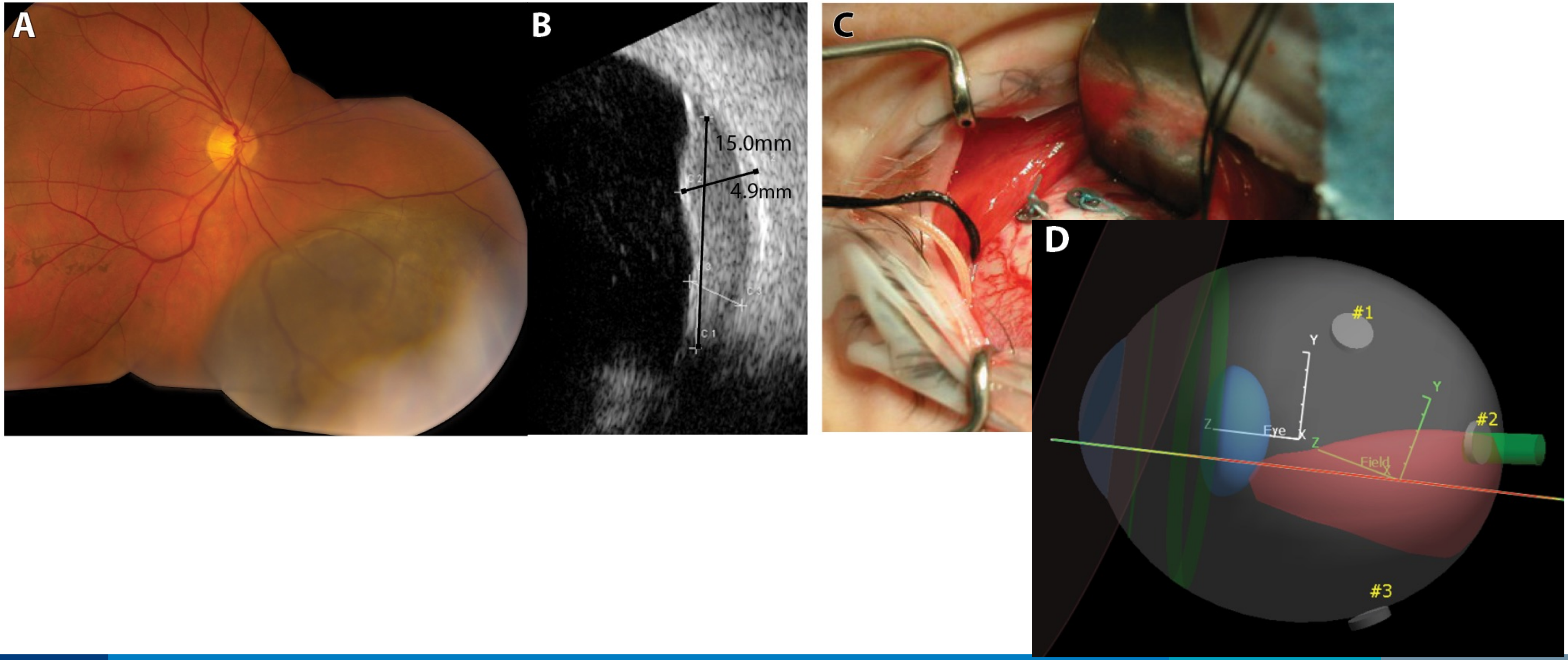


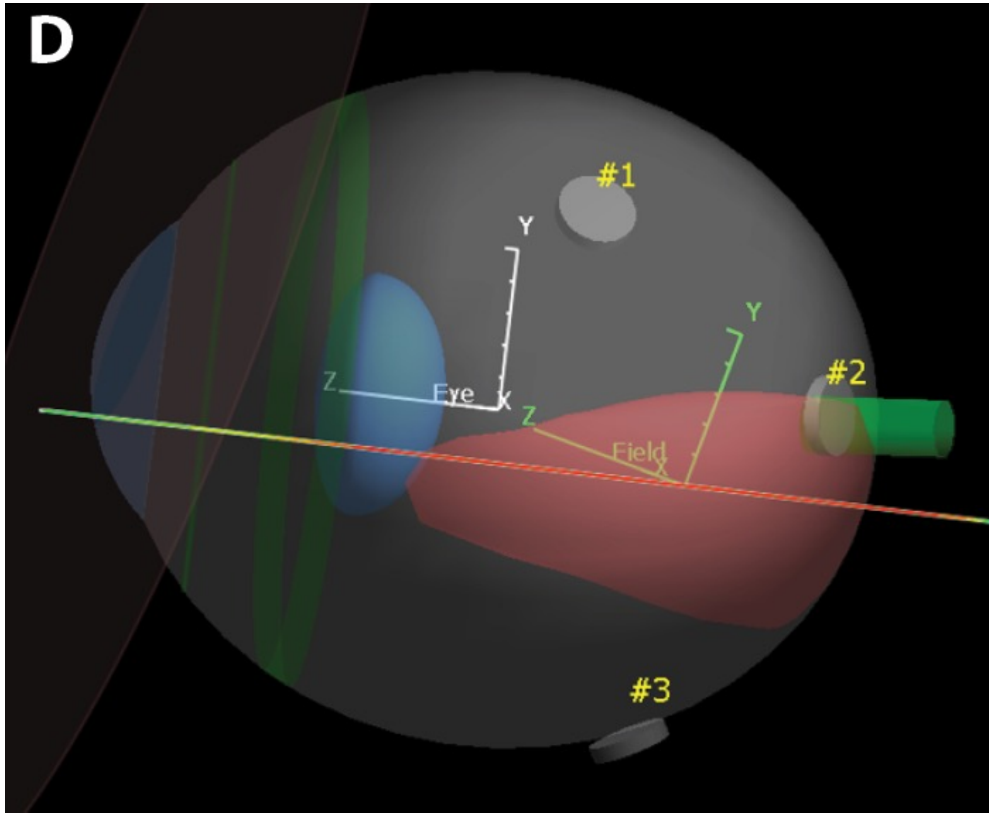
A.
Superior
Cornea
Nasal
Central
Temporal
Cornea
Inferior
F.
RMS
Distance (mm)
0.4
0.2
0.0
−0.2
−0.4

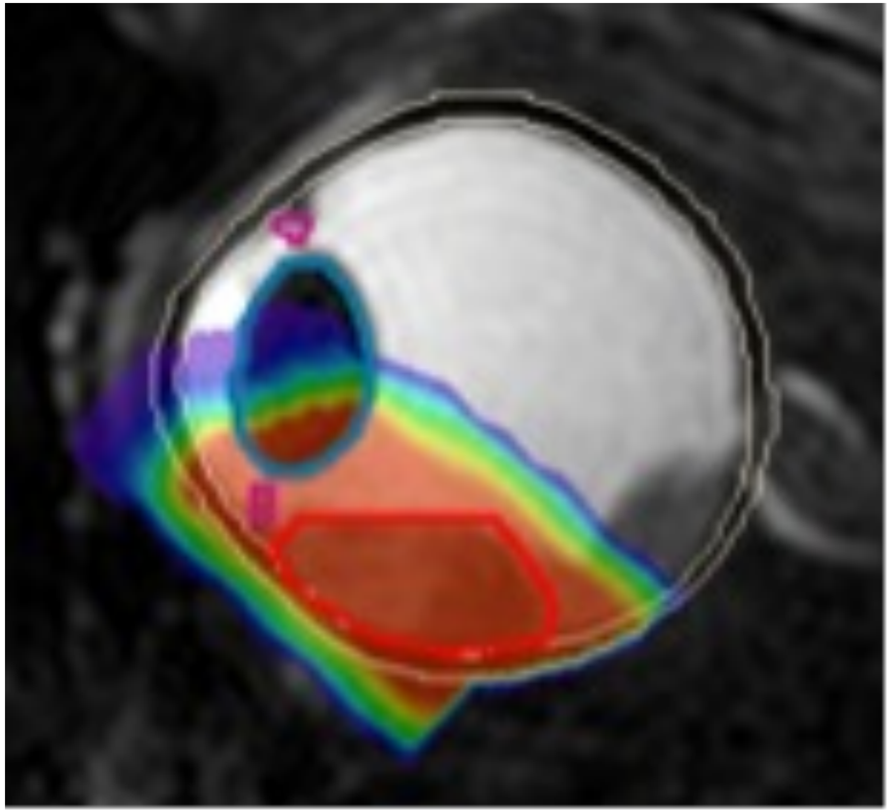
Radiotherapieplanning

Protonen therapie

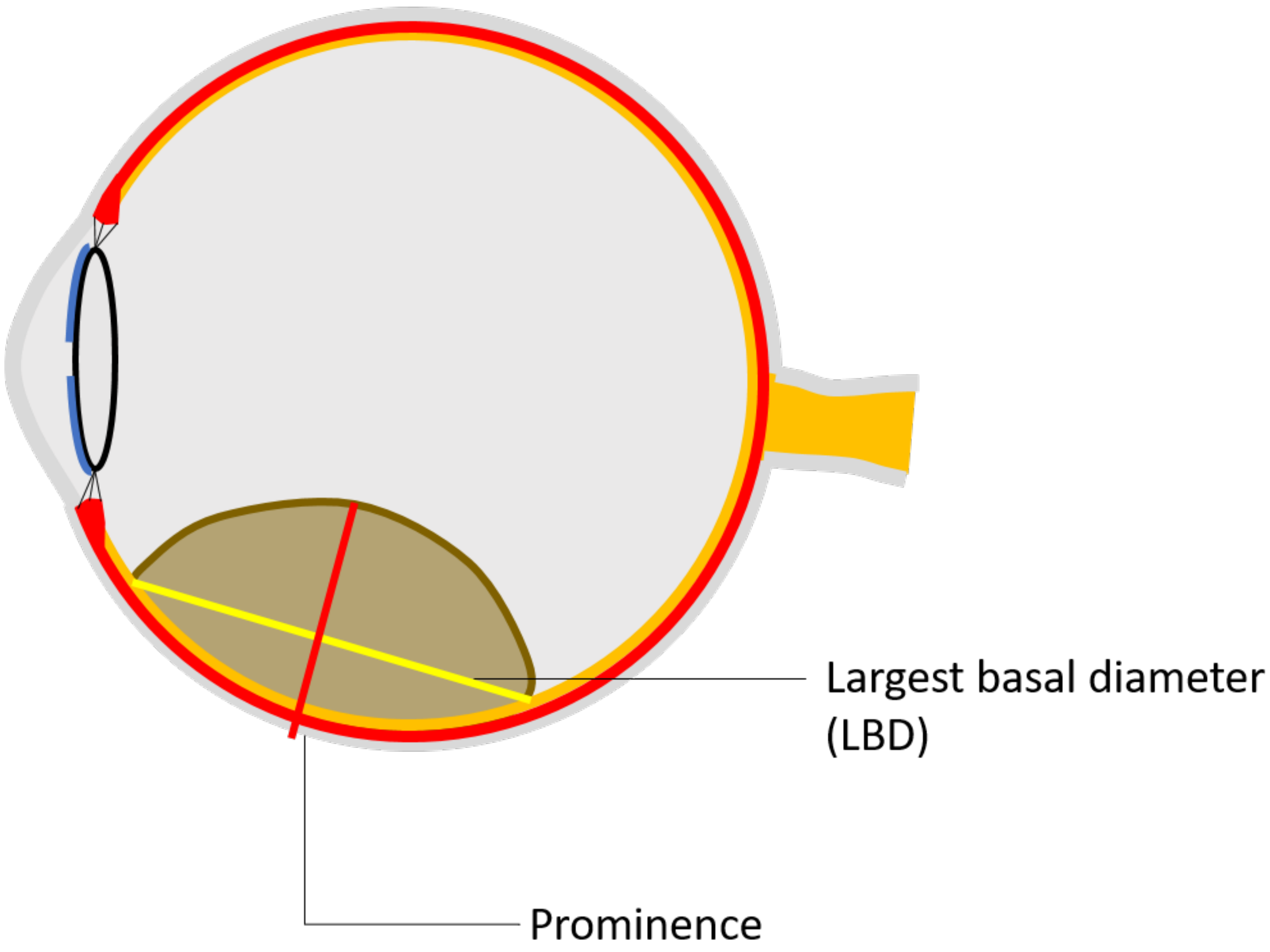
Goede resultaten (>95% lokale controle), maar veel zichtverlies

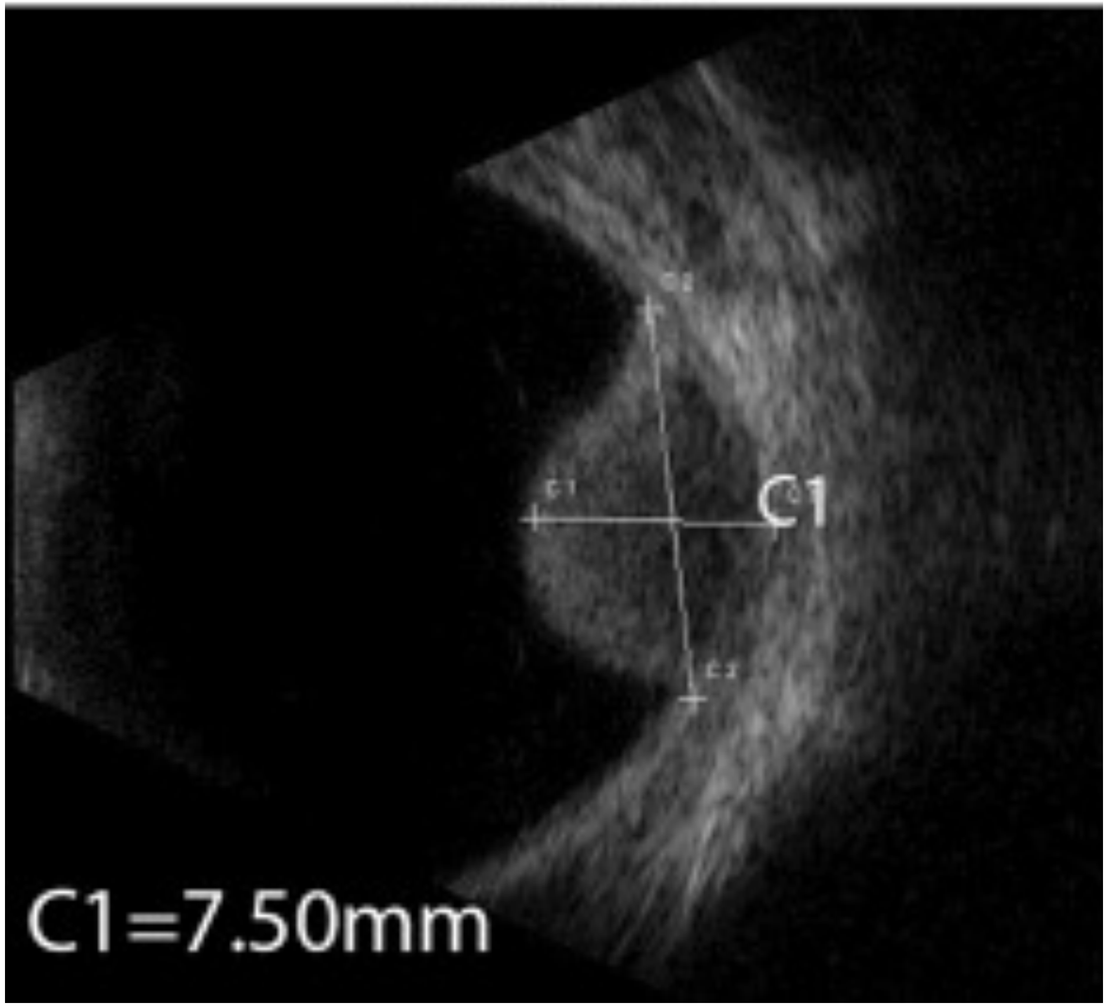



D
#1
Y
Y
#2
Z
Eye
X
Z
Field
X
#3

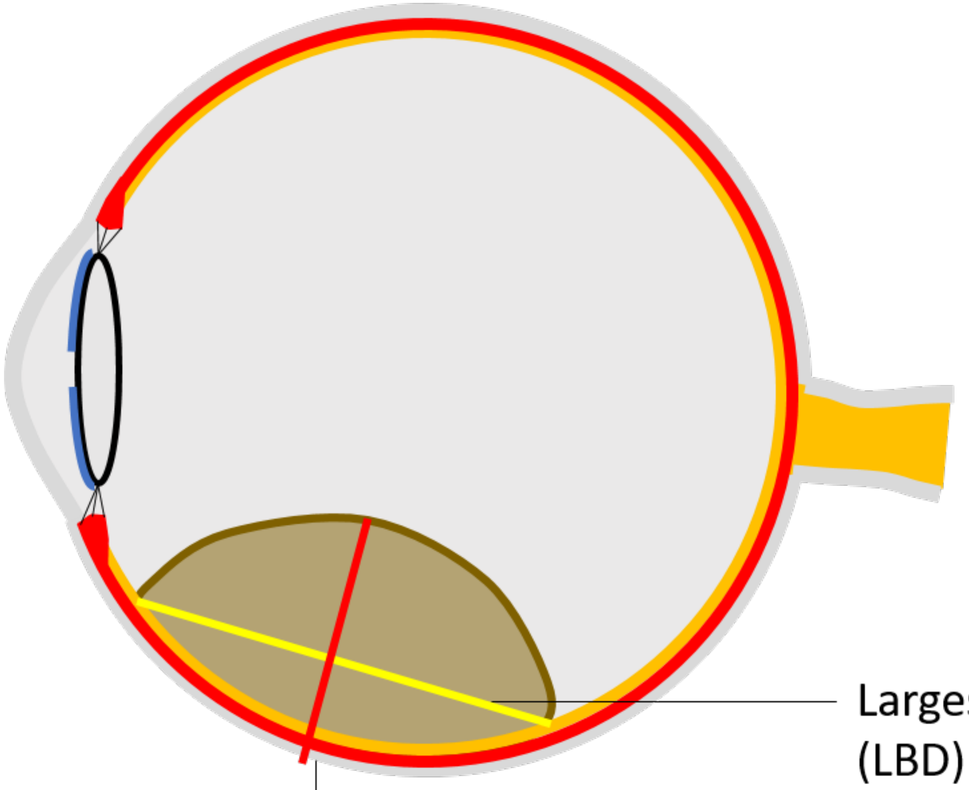


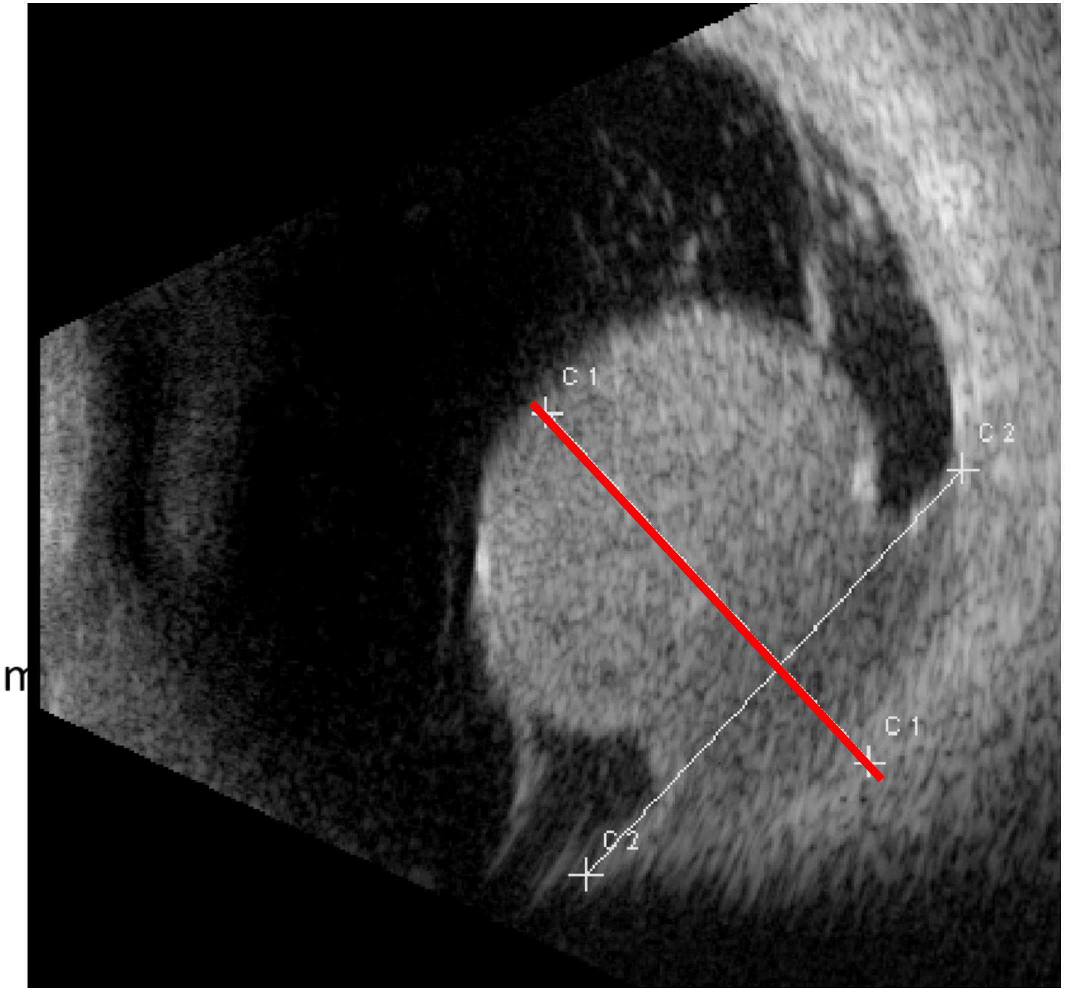
3D tumor afmetingen



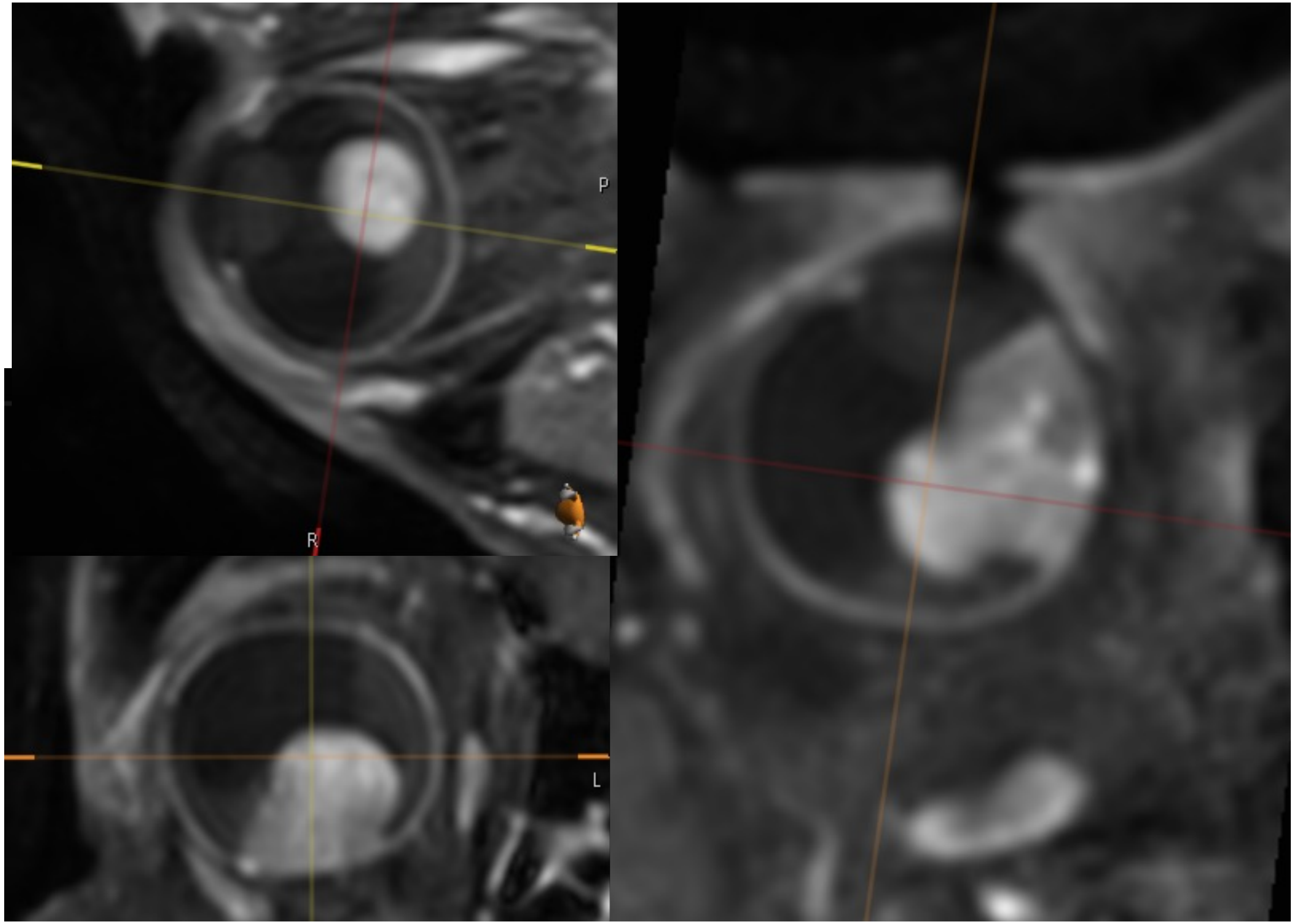


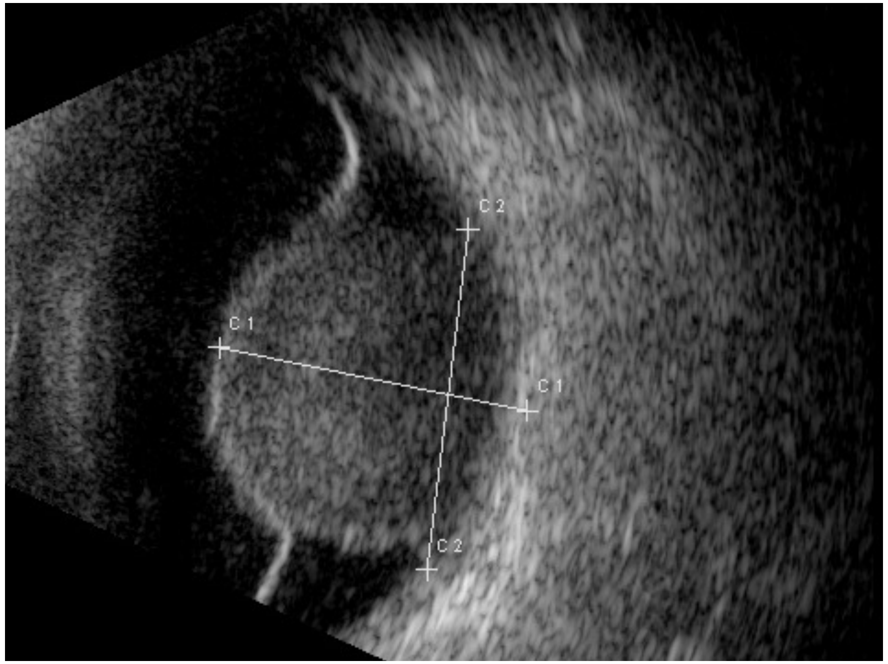
3D tumor afmetingen



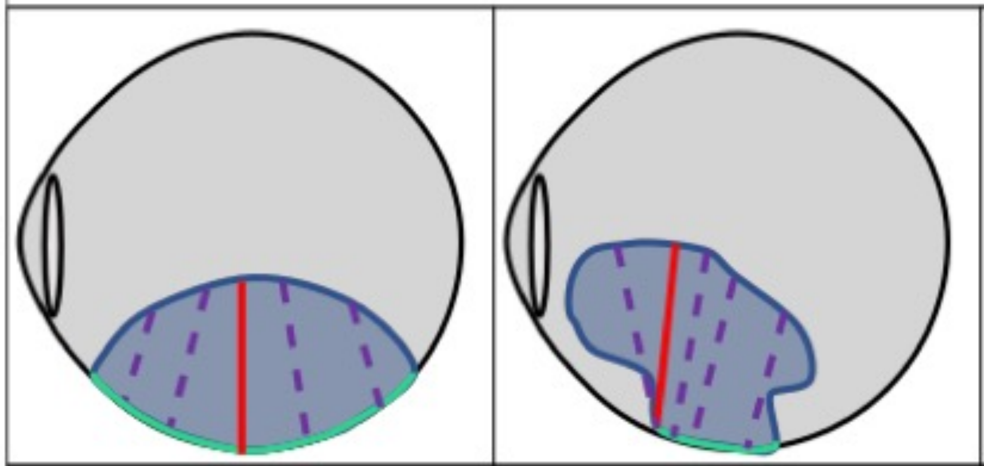
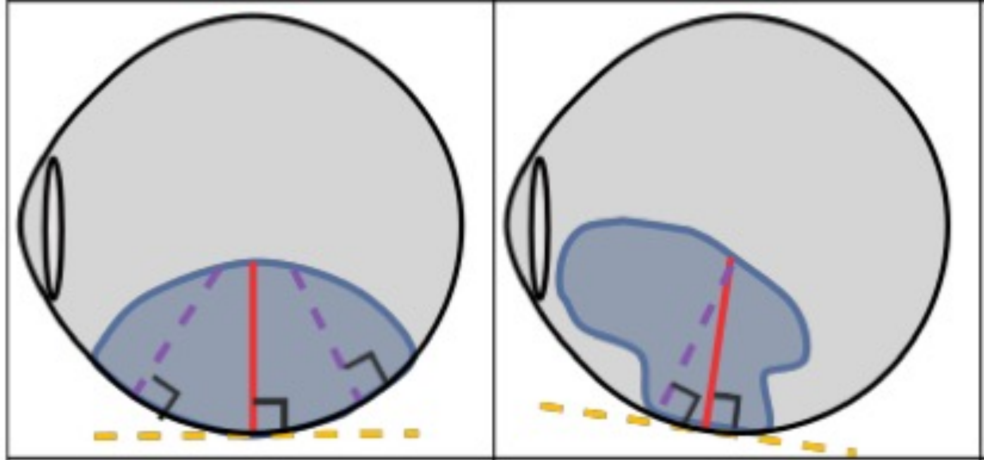
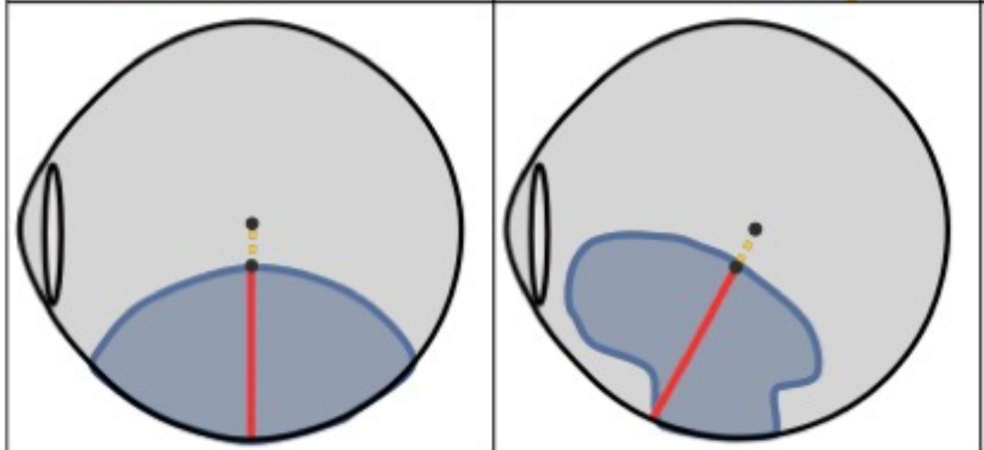


3D tumor afmetingen

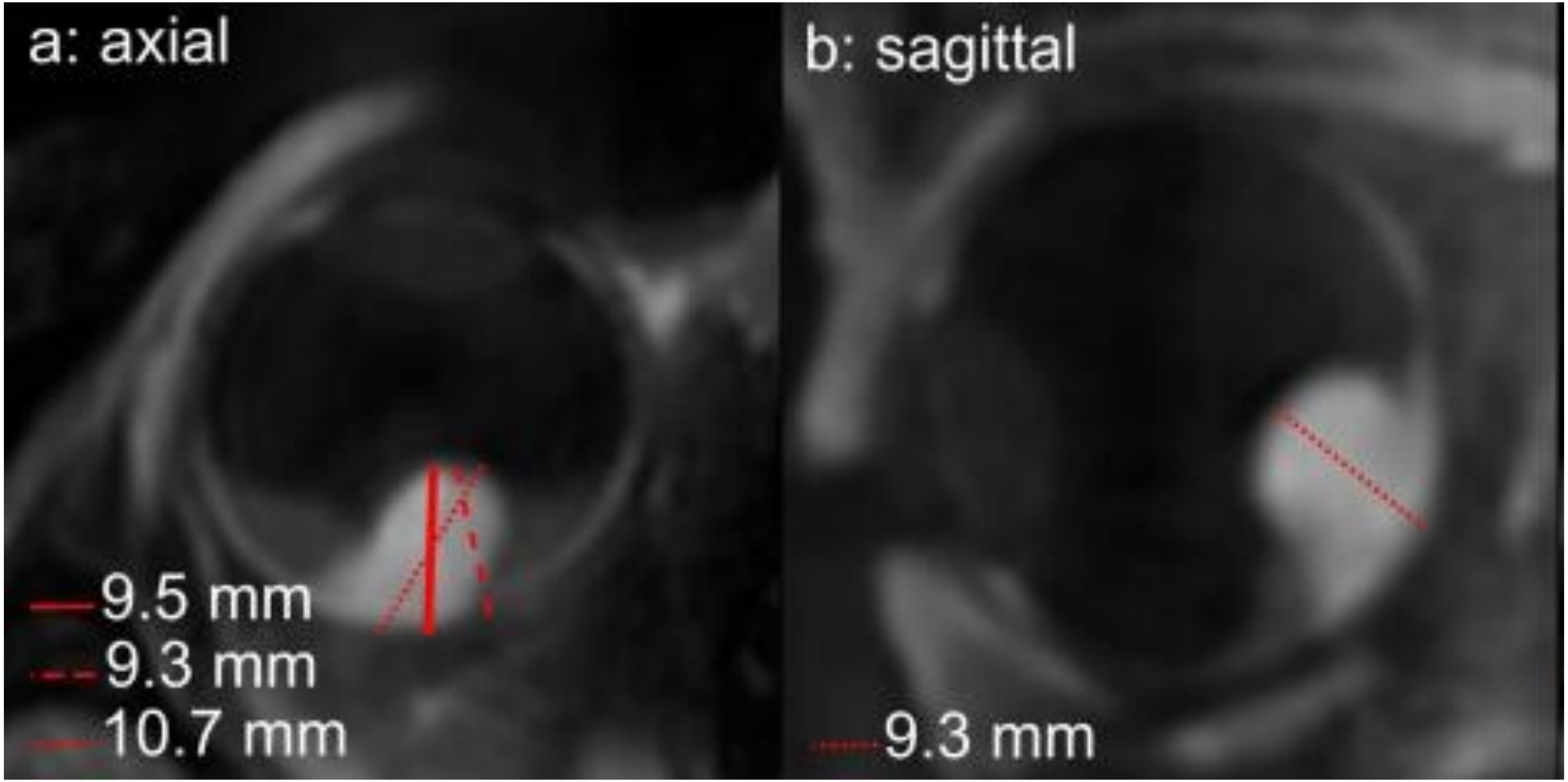




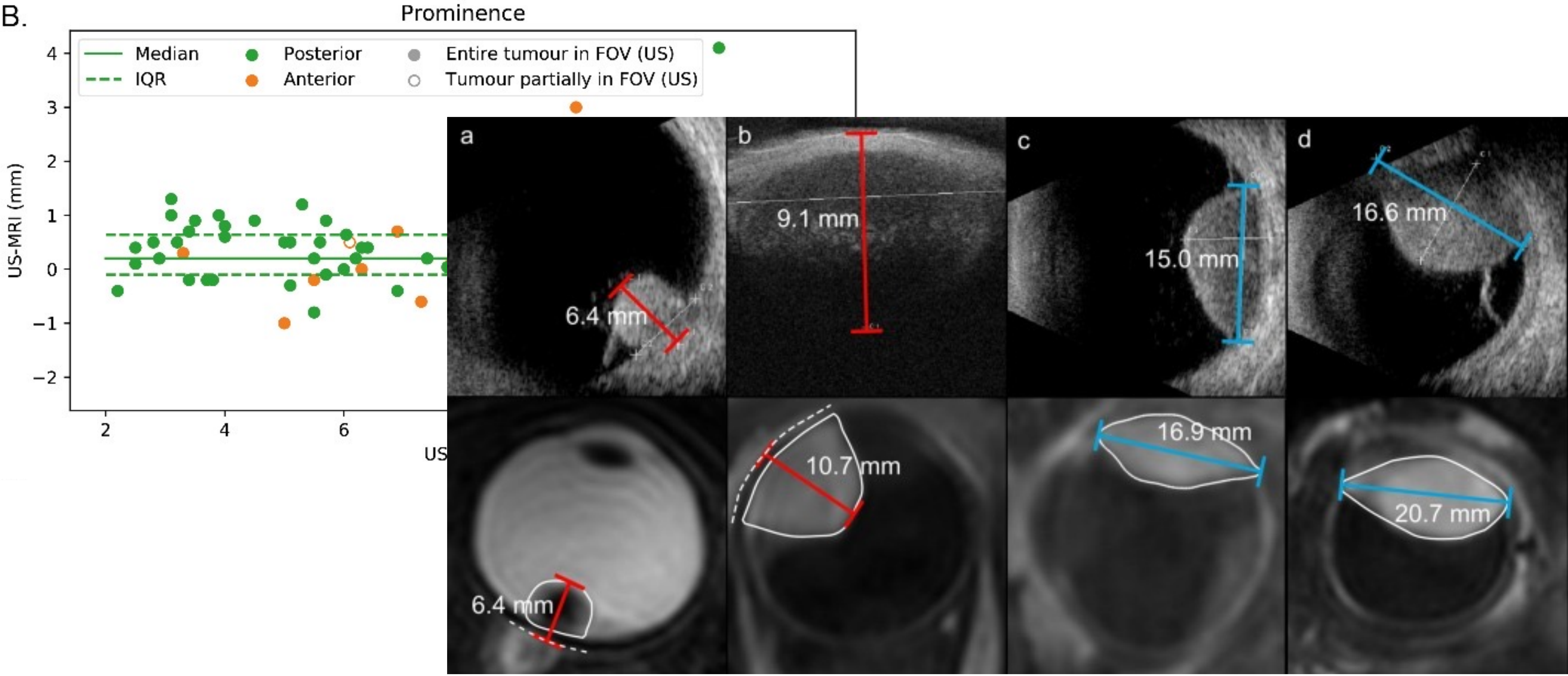
3D

Prominence definitions	
	**Hausdorff distance** Maximum of all minimum distances between all points in tumour base (green) and top.
	**Sclera-based definition** Largest distance between tumour top and base, perpendicular to the sclera.
	**Centre-based definition** Distance between tumour apex and base, measured along the line between vitreous' centre of mass and tumour apex, where tumour apex is defined as the point of the tumour closest to the centre of the vitreous.

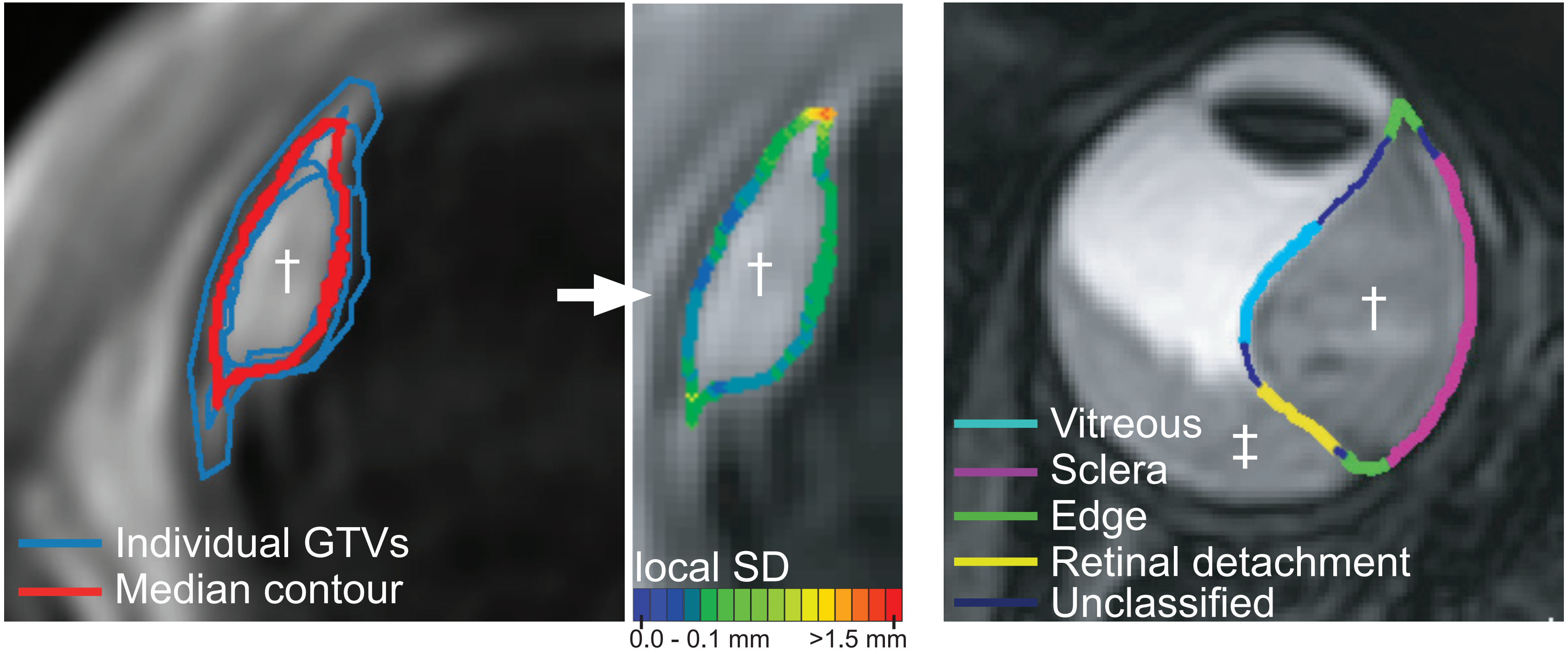
3D tumor afmetingen

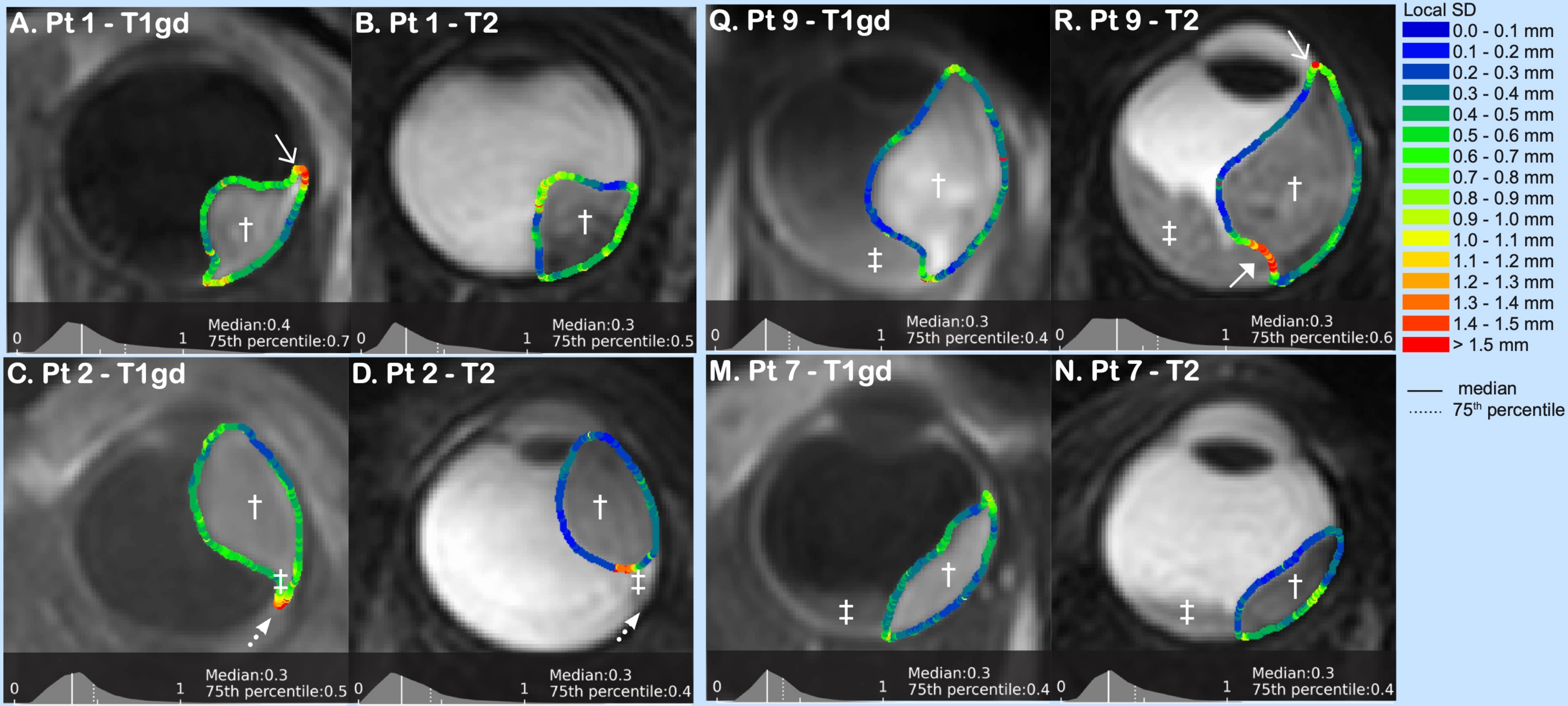


Accuratie MRI



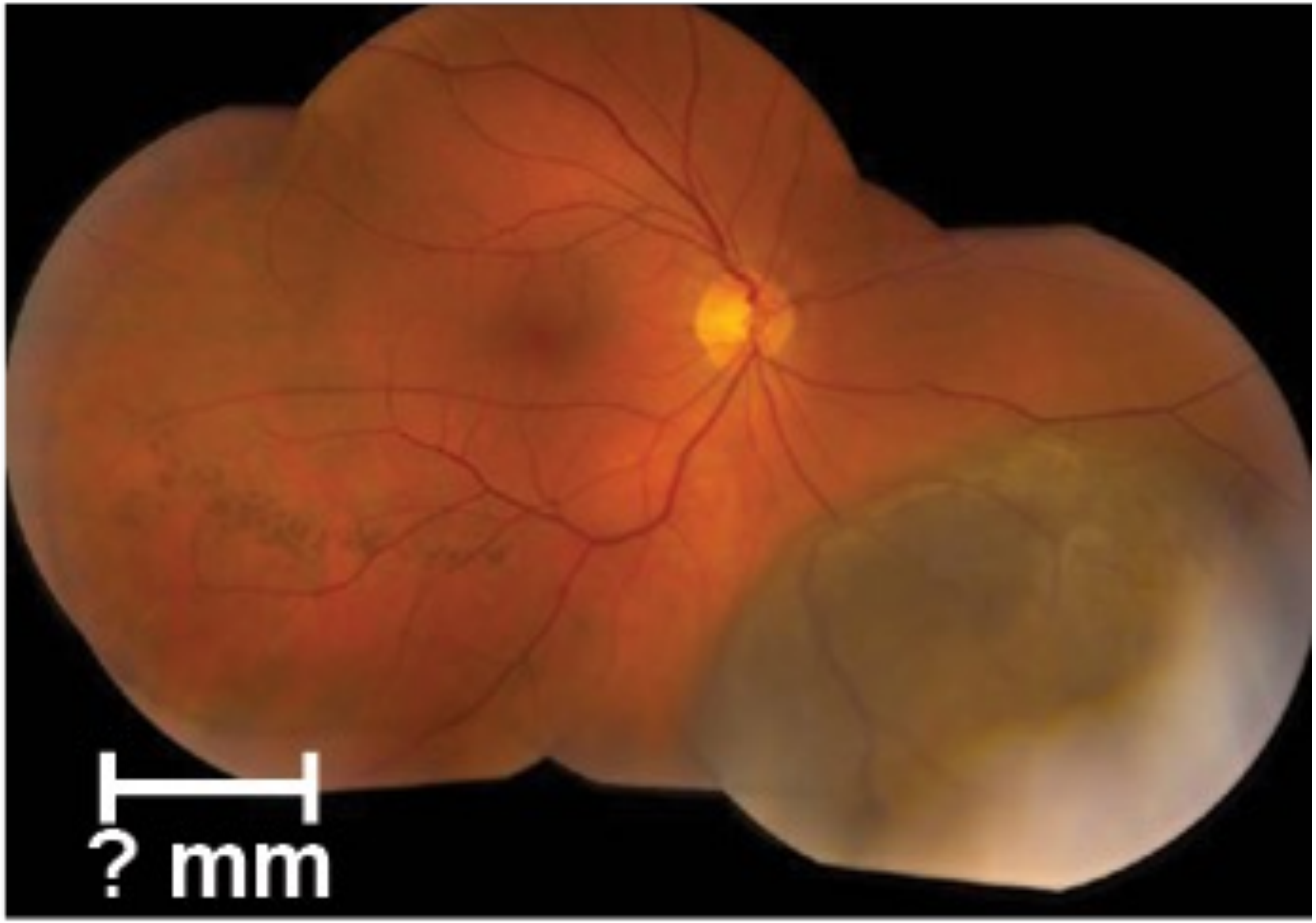
Accuratie MRI

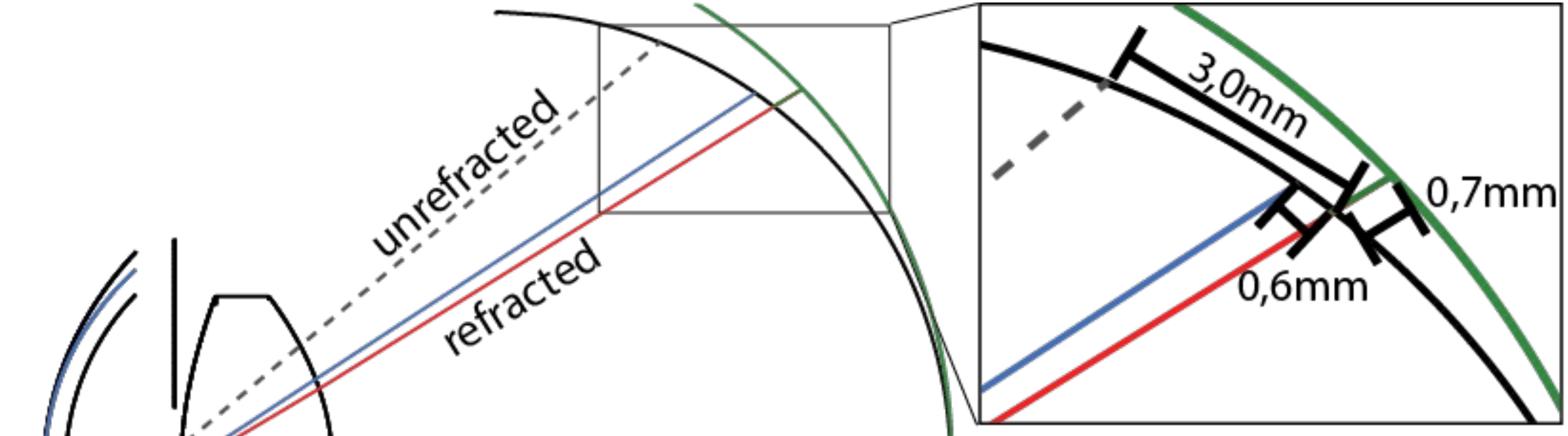


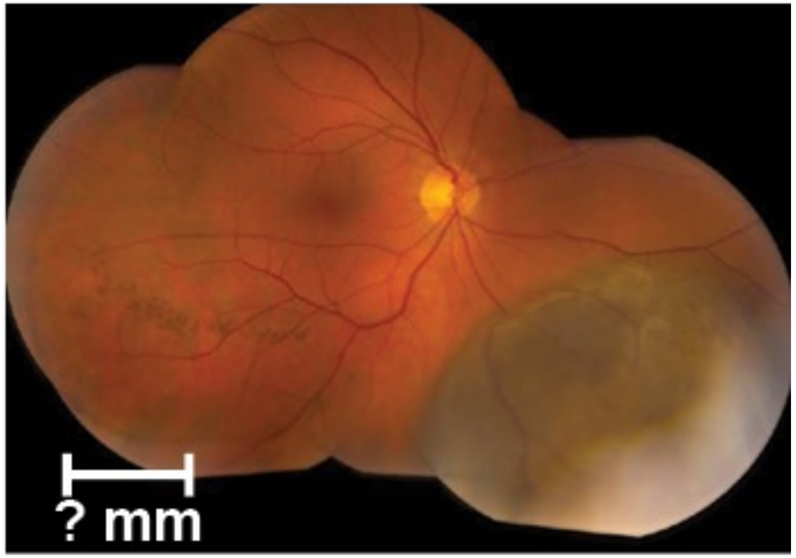


A. Pt 1 - T1gd
B. Pt 1 - T2
Q. Pt 9 - T1gd
R. Pt 9 - T2
Median:0.4
75th percentile:0.7
Median:0.3
75th percentile:0.5
Median:0.3
75th percentile:0.4
Median:0.3
75th percentile:0.6
C. Pt 2 - T1gd
D. Pt 2 - T2
M. Pt 7 - T1gd
N. Pt 7 - T2
Median:0.3
75th percentile:0.5
Median:0.3
75th percentile:0.4
Median:0.3
75th percentile:0.4
Median:0.3
75th percentile:0.4
Local SD
0.0 - 0.1 mm
0.1 - 0.2 mm
0.2 - 0.3 mm
0.3 - 0.4 mm
0.4 - 0.5 mm
0.5 - 0.6 mm
0.6 - 0.7 mm
0.7 - 0.8 mm
0.8 - 0.9 mm
0.9 - 1.0 mm
1.0 - 1.1 mm
1.1 - 1.2 mm
1.2 - 1.3 mm
1.3 - 1.4 mm
1.4 - 1.5 mm
> 1.5 mm
median
75th percentile

Optical imaging




unrefracted
refracted
3,0mm
0,7mm
0,6mm


? mm

Acknowledgements

- Radiology
  - T. Ferreira
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  - K. Keene
  - L. van Vught
- Philips Healtcare
  - M. Versluis
  - P. de Bruin

Als fysicus in een ziekenhuis – enkele reflecties

- "eenvoudige" natuurkunde kan direct klinische impact hebben
  - maar wordt vaak over het hoofd gezien
  - wel veel nieuwe kansen (klinische technologie, technische geneeskunde, medical enginering,…)
- Experimenteel vaak uitdagend, want je hebt geen volledige controle over je "sample"

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