High Resolution MR EYE Protocol Optimization and Perspectives

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MR-EYE background

- **MRI System:**
  - 0.5T- 11.7T
- **MRI-Eye protocol:**
  - High resolution 3D T1-weighted (pre- and post-contrast imaging)
  - 2D or 3D T2 turbo spin echo techniques with low Echo Train Length (ETL: 5-10)
- **Contrast Agents:**
  - Magnevist (Gd-DTPA)
  - Manganese ($MnCl_2$)
  - Iron Oxide Nanoparticles
- **Injection pathways:**
  - Intravenous
  - Intravitreal
  - Subconjunctival
  - Eyedrops
- **MR-Eye applications:**
  - Anatomical study
  - Structural assessment of eye diseases
  - Functional MRI of the retina (BOLD-effect)
  - Ocular drug delivery

Historical review

- ***First study:***

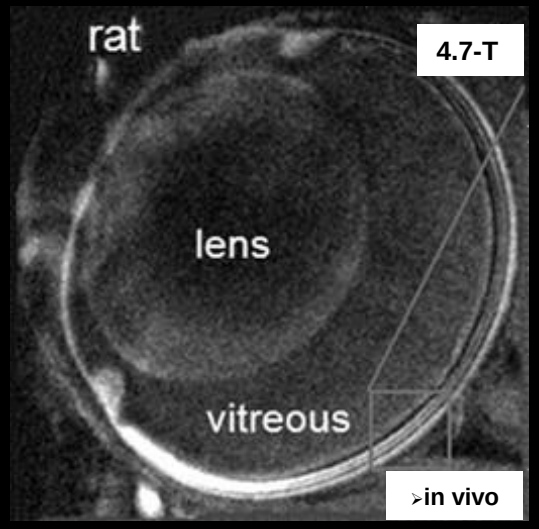
  "Opening of blood-ocular barrier demonstrated by contrast-enhanced MR imaging." Frank JA et al., J Comput Assist Tomogr. 10(6):912-6, **1986**.

- ***Eye anatomy 1.5-T MRI***

  "Demonstration of an anterior diffusional pathway for solutes in the normal human eye with high spatial resolution contrast-enhanced dynamic MR imaging." Bert RJ et al., Invest Ophthalmol Vis Sci. 47(12):5153-62, **2006**.

- ***Eye anatomy 4.7-T MRI***

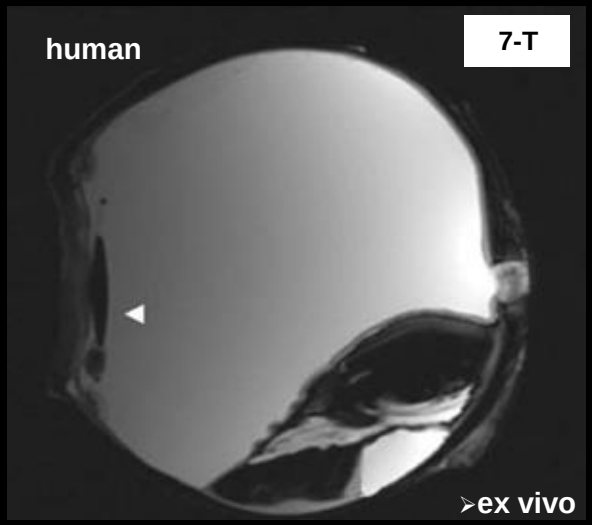
  "Manganese enhanced MRI reveals multiple cellular and vascular layers in normal and degenerated retinas." Nair G. et al., J Magn Reson Imaging. 2011 Dec;34(6):1422-9, **2011**.



Historical review

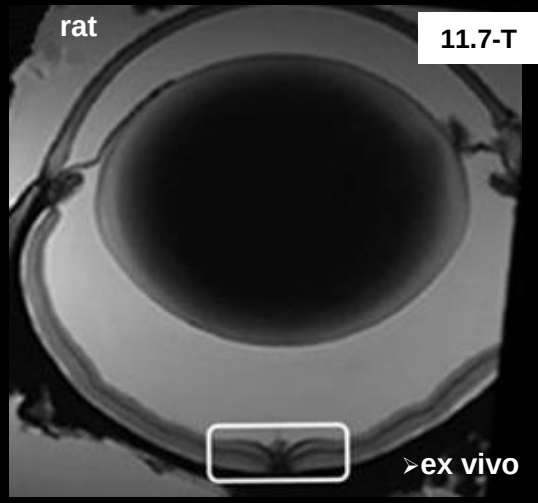
- ***Eye anatomy 7-T MRI***

  "Experimental differentiation of intraocular masses using ultrahigh-field magnetic resonance imaging-A case series." Falke K. et al., PLoS One.8(12):e81284, **2013**.



- ***Eye anatomy 11.7-T MRI***

  "3D magnetic resonance microscopy of the ex vivo retina." De La Garza BH et al, Magn Reson Med. 67(4):1154-8., **2012**.



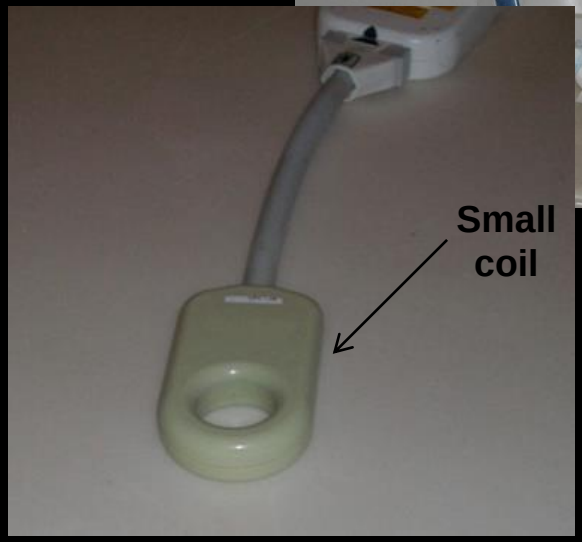
MR-EYE study - Objectives

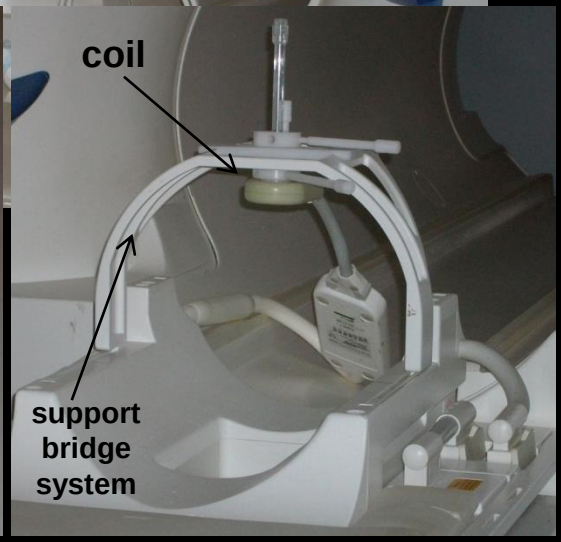
❖ *The purpose of this study was to compare selected pulse sequences for MRI of the eye and to evaluate their potential for the depiction of specific anatomic regions.*

❖ **MRI system:**

- 1.5-T MRI clinical system
- utilizing both a head or body coil
- small surface coil
- high-resolution (100x100x600µm)

Clinical MRI System 1.5 T





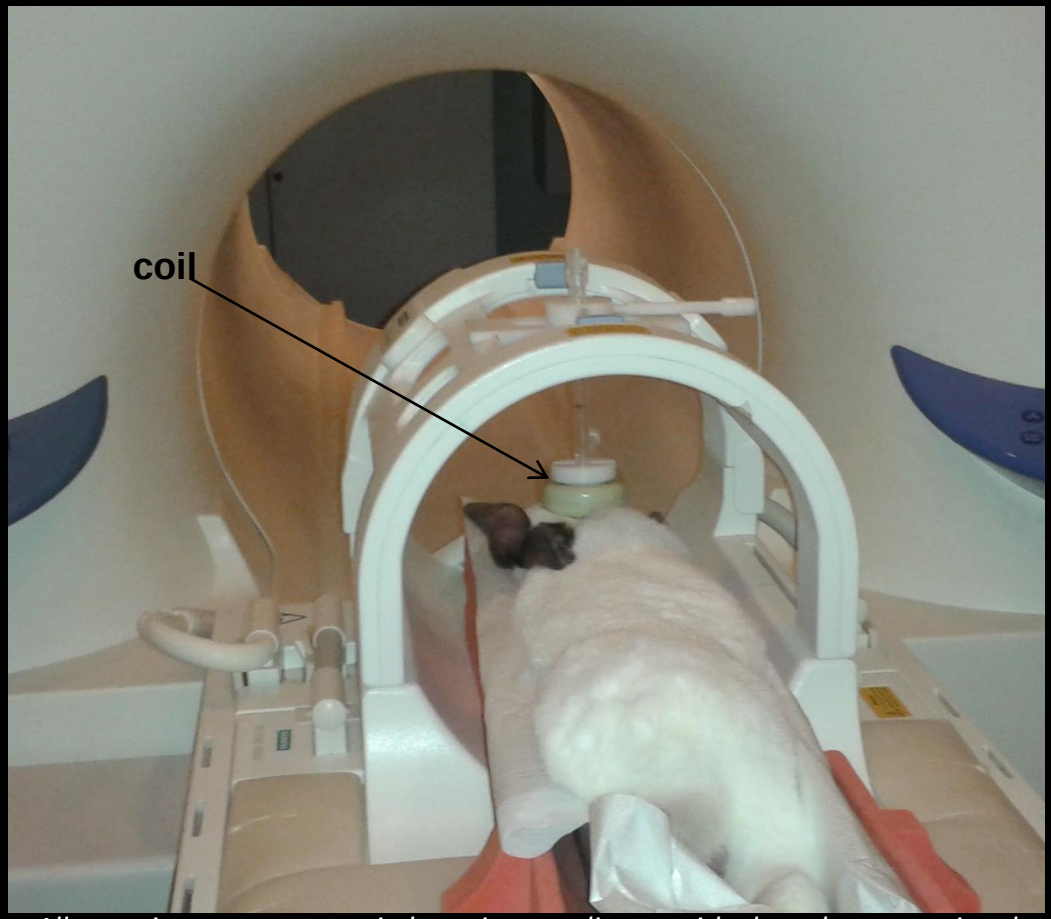
Clinical MRI System – 3D MR EYE Imaging

❖ **Animal's anesthetization:**

- experimental animal: rabbit
- subcutaneous Injection of a mixture of 2.5 ml xylazine ketamine hydrochloride (5 mg/ kg) and 1.5 ml ketamine hydrochloride (50 mg/ kg)

❖ **MR-Eye contrast agent:**

Magnevist (Gd-DTPA) 0.5 M:
Intravenous injection 0.2 ml/kgr body weight



All experiments were carried out in compliance with the relevant national laws relating to the conduct of animal experimentation.

Sequence Parameters

- **3D (T2/T1)w sequences:**
  - reverse fast imaging with steady state precession (3D-PSIF)
  - constructive interference in steady state (3D-CISS)

- **3D T1w sequence:**

  volumetric interpolated breathold examination (3D-VIBE)

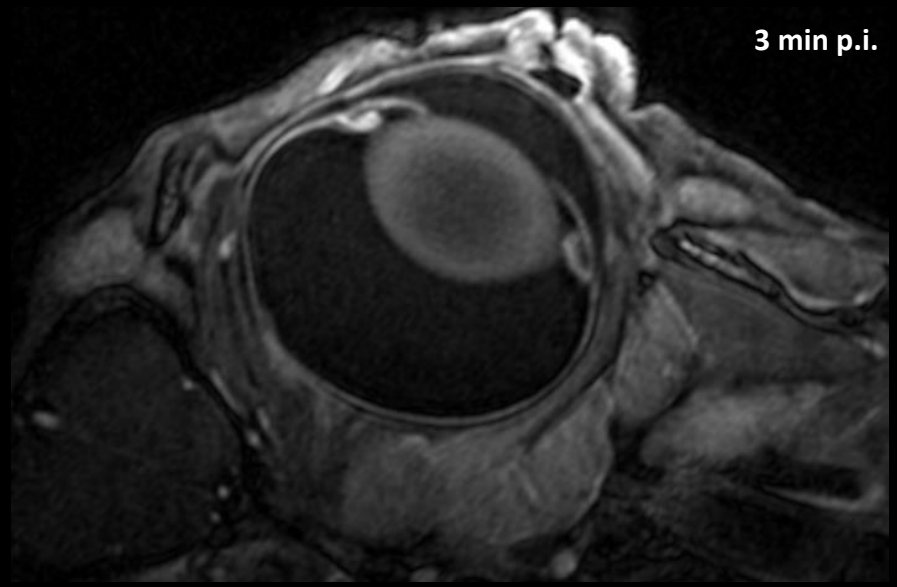
Parameters	3D-PSIF	3D-CISS	3D-VIBE
Slice thickness (µm)	600	600	600
No. of slices	30	30	30
Field of view (mm)	60	60	60
In plane Resolution (µm)	78	78	94
TR (ms)	20.92	12.98	11.80
TE (ms)	10.19	5.5	5.02
Flip angle (°)	70	70	15
Scan time per volume (min)	**3.10**	**3.40**	**3.50**

I. Tsiapa, et al. "*High Resolution MR eye protocol optimization: comparison between 3D-CISS, 3D-PSIF and 3D-VIBE sequences*" (*Physica Medica*: *European Journal of Medical Physics*, Published online: April 10, 2015).

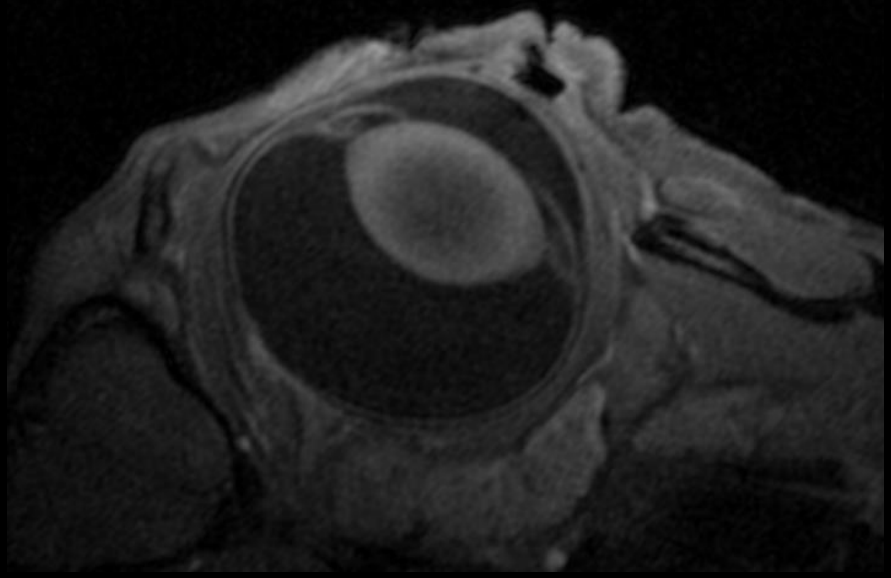
3D-VIBE (T1w sequence)

Post Gd-DTPA

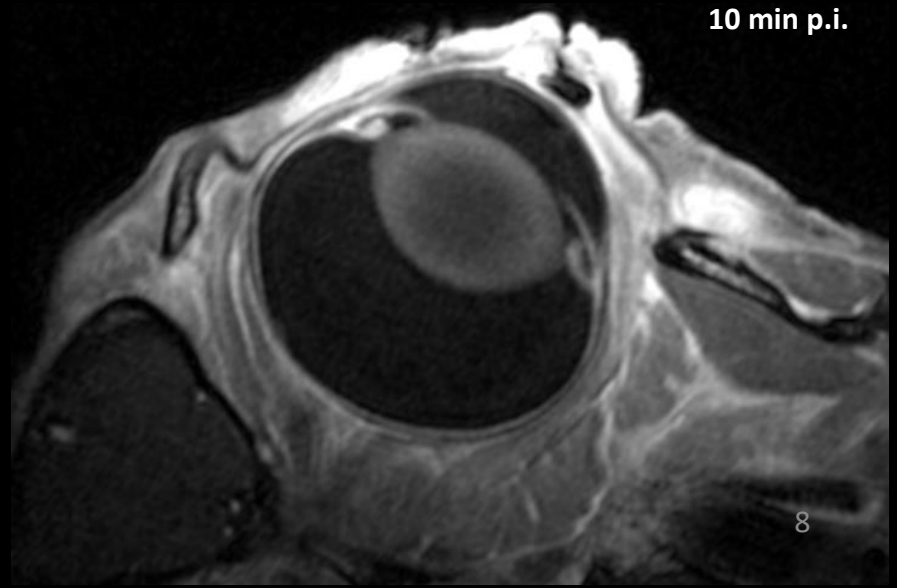
3 min p.i.



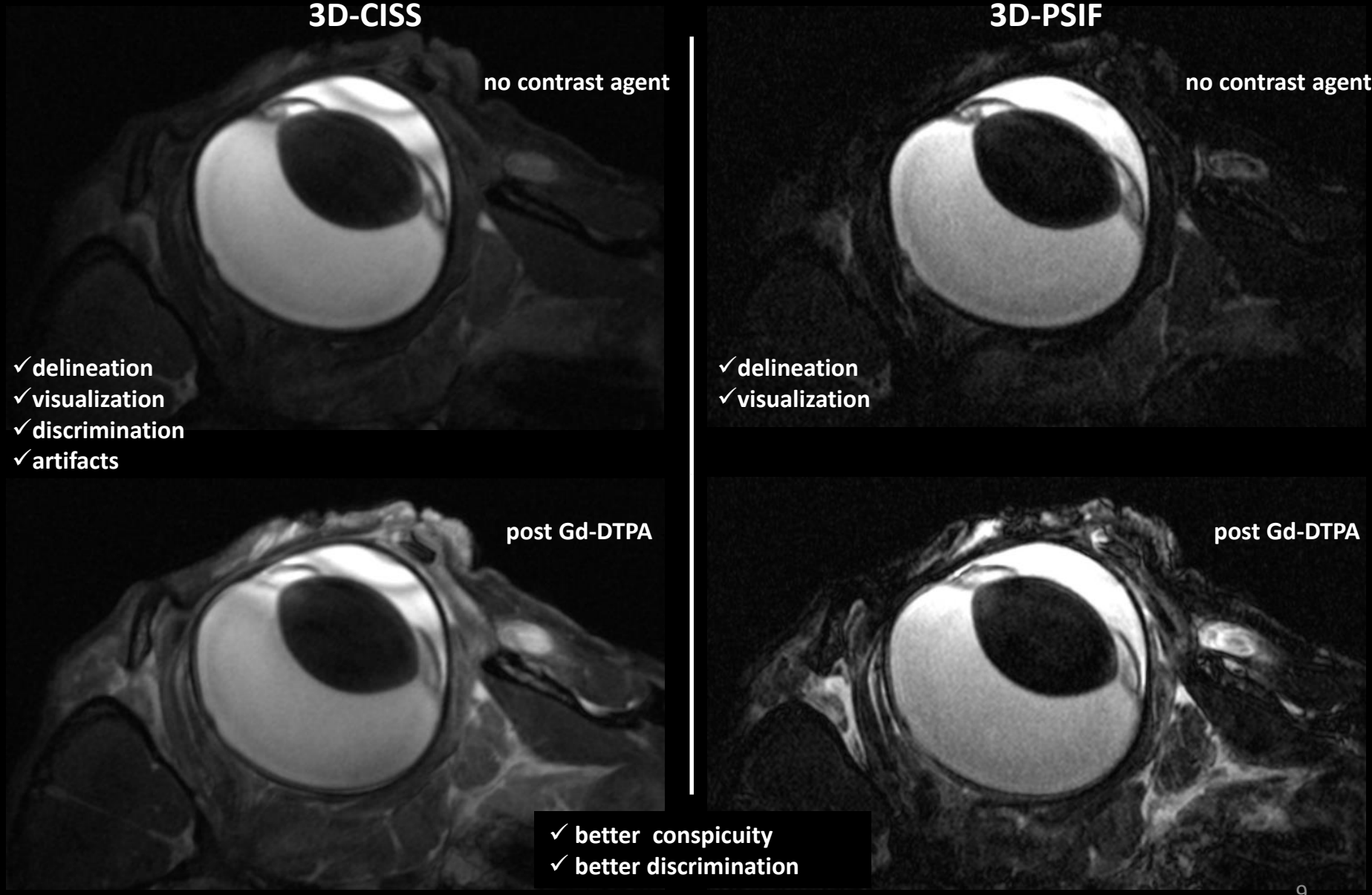
no contrast agent



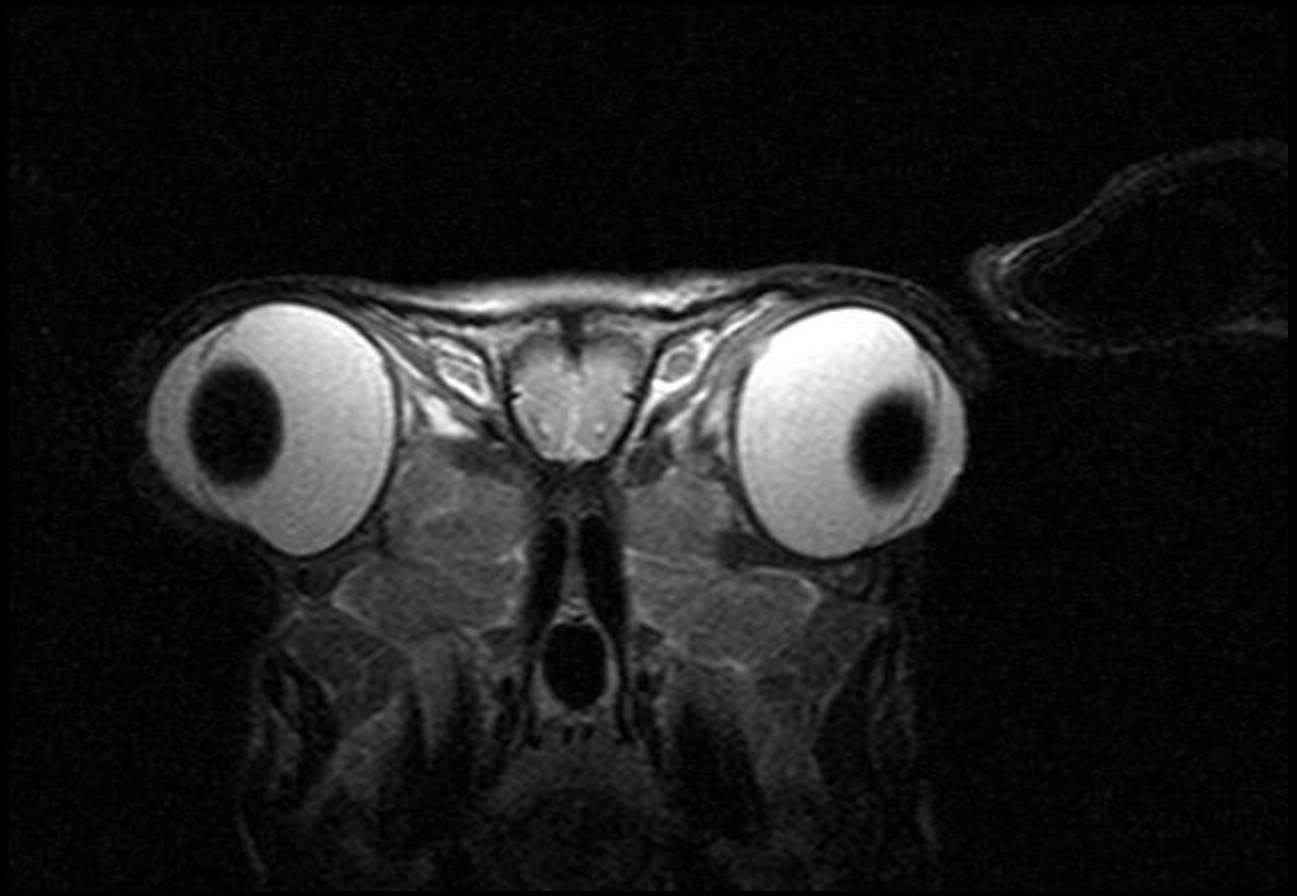
10 min p.i.



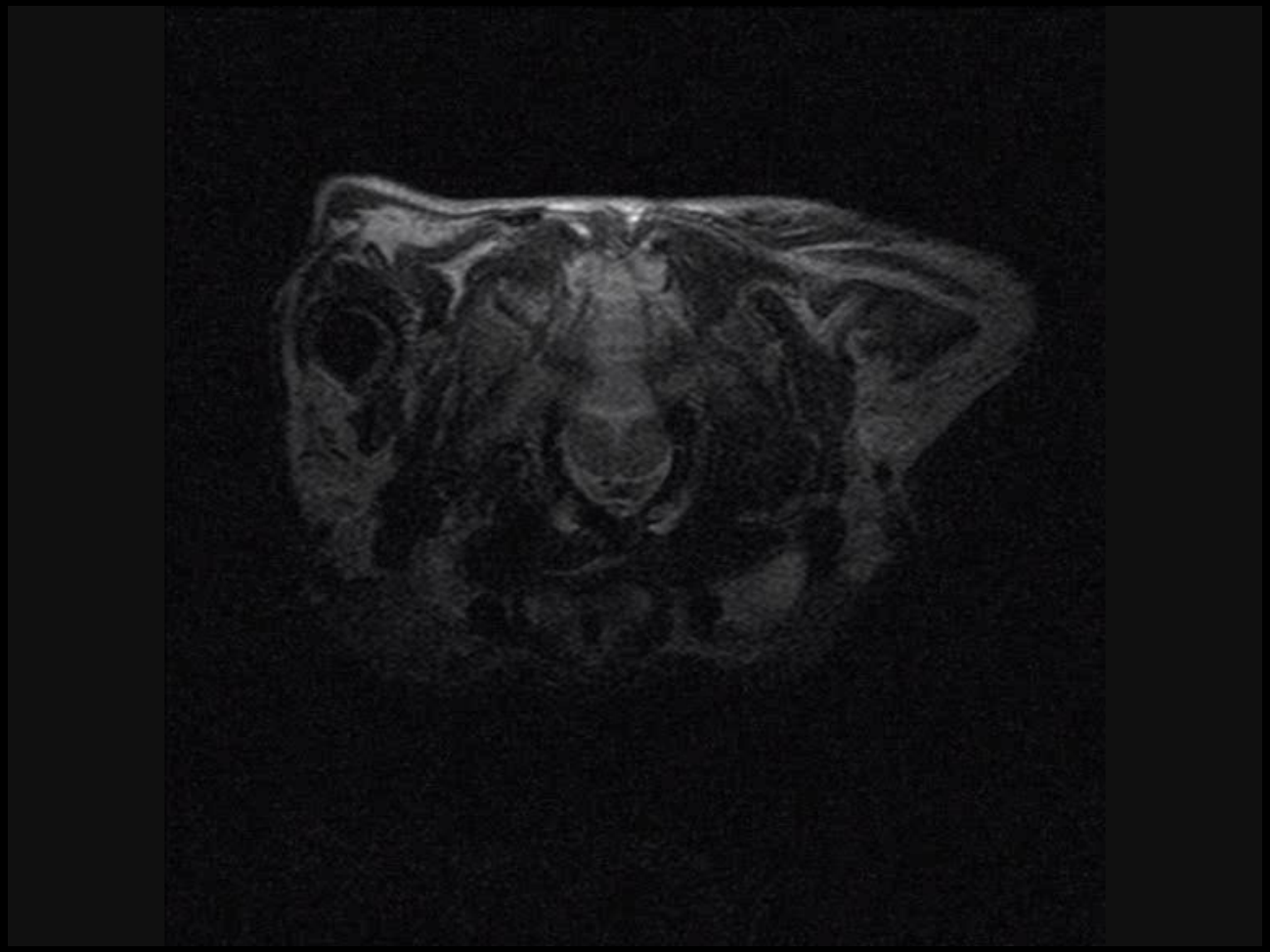
3D T2/T1w sequences



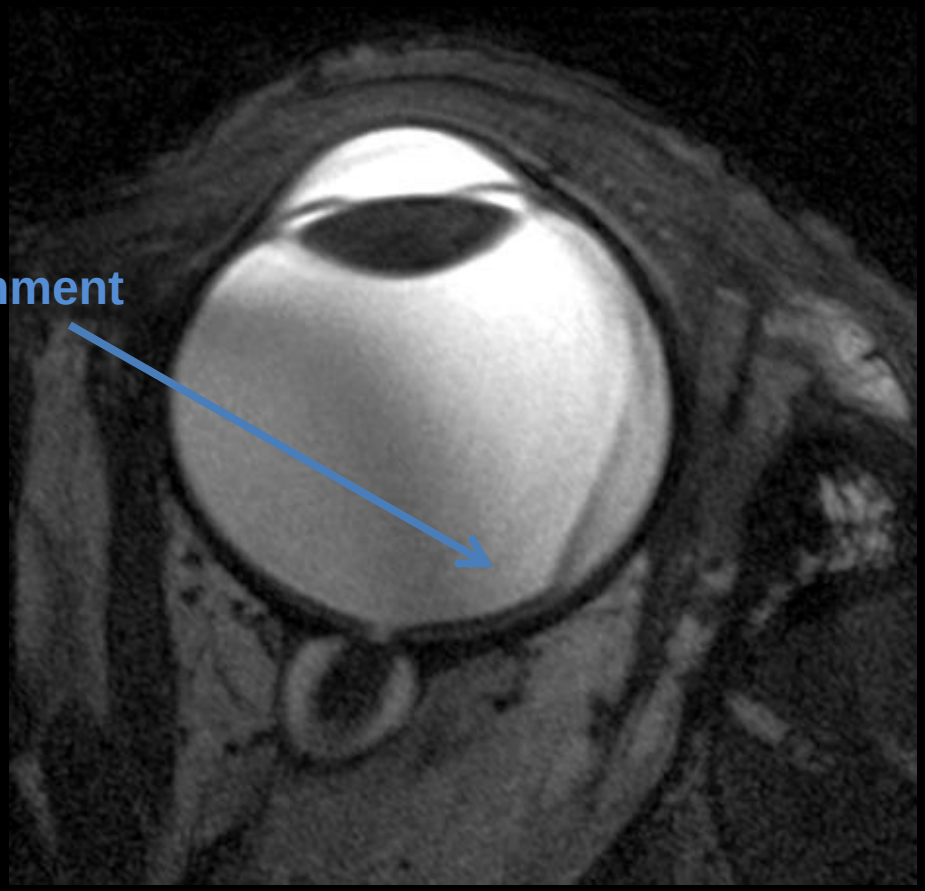
MR EYE Protocol - Results



MR EYE Protocol - Results



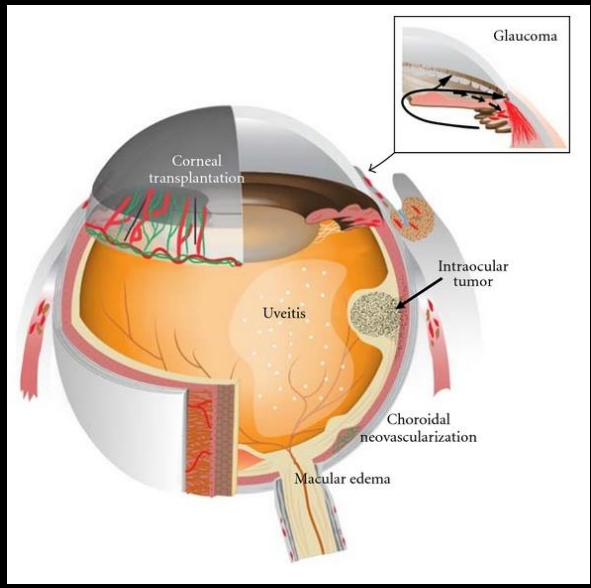
Clinical MRI Study



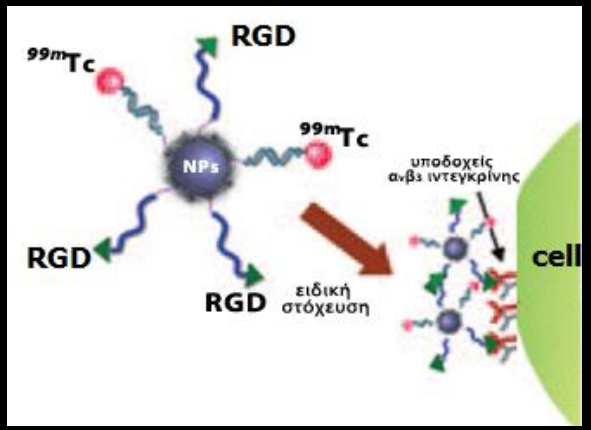
MRI of Ocular Angiogenesis

MR-EYE background

- **Angiogenesis related diseases:**
  - diabetic retinopathy
  - age-related macular degeneration

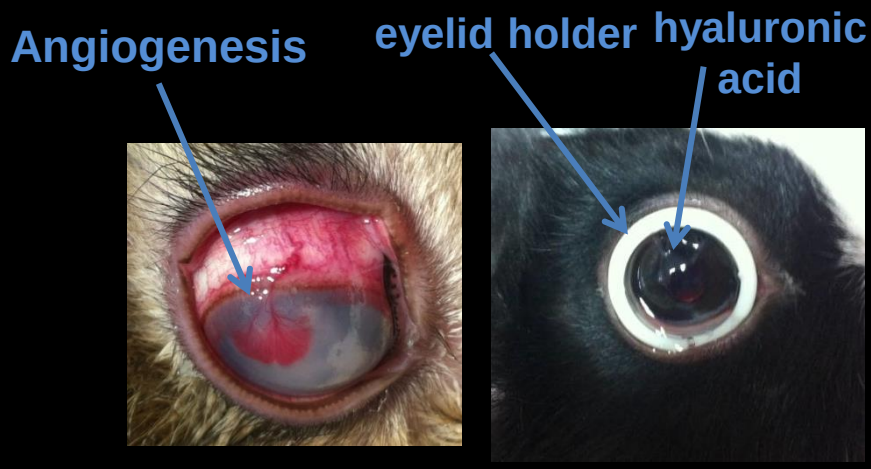


- **MRI of Ocular Angiogenesis:**
  - targeted NPs



Angiogenesis Protocol

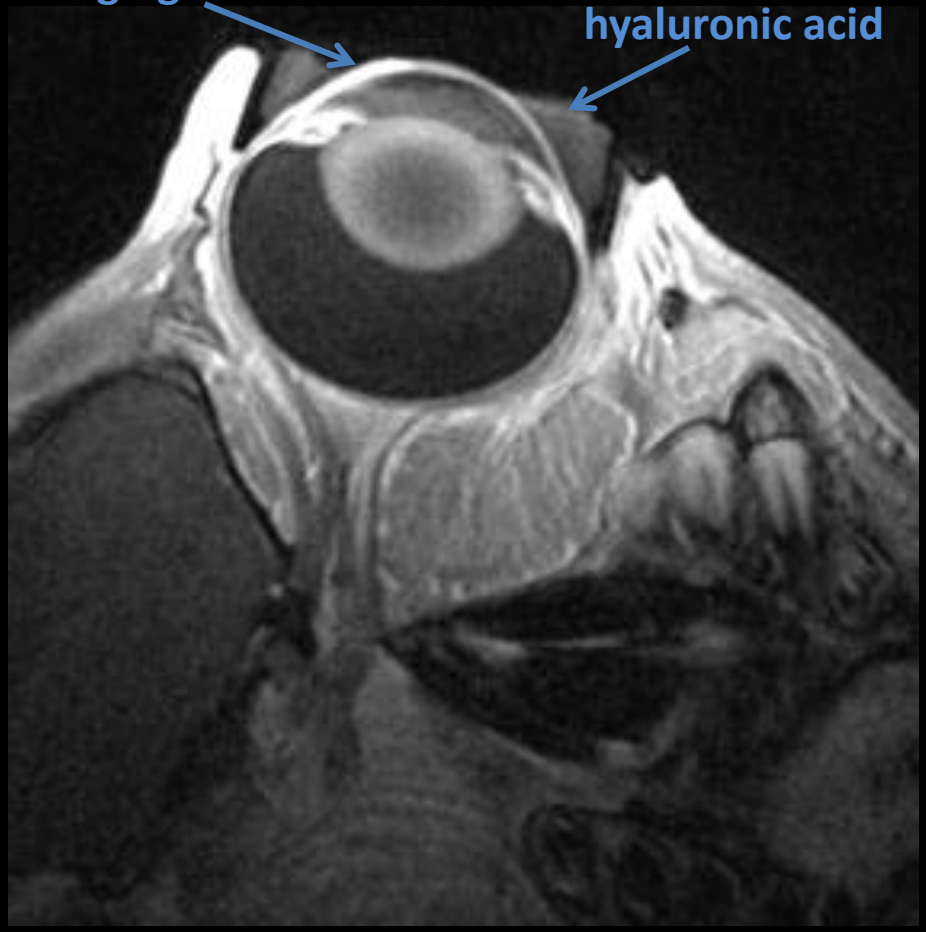
- **experimental animal:** rabbit
- **General anesthesia:** subcutaneous Injection of a mixture of 2.5 ml xylazine ketamine hydrochloride (5 mg/ kg) and 1.5 ml ketamine hydrochloride (50 mg/ kg)
- **Local anesthesia:** was achieved using topical proparacaine (Alcaine; Alcon)
- **Induction of Corneal Neovascularization:** A corneal suture passing through the stroma was made with a 3-mm long 7-0 black silk.
- The suture was removed when neovascularization was fully developed.
- Appropriate eyelid holder and hyaluronic acid for MR imaging of corneal angiogenesis.



3D-MR Imaging of Corneal Angiogenesis:
2ml Intravenous injection (500mM Gd-DTPA)

Pre-contrast

Post-contrast



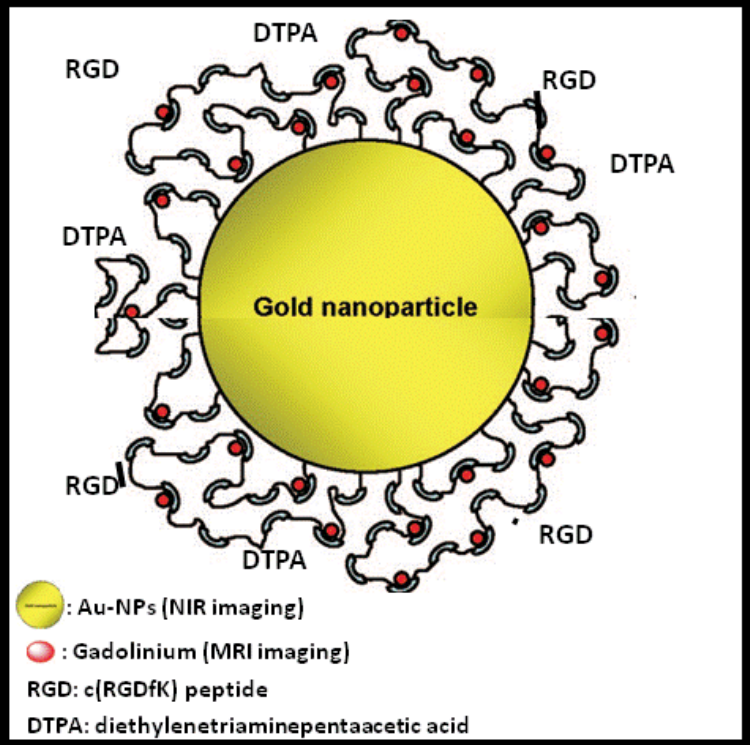
3D-MR Imaging of Corneal Angiogenesis:
2ml Intravenous injection of Magnevist (500mM Gd-DTPA)

MRI of Corneal Angiogenesis using Nanoparticles

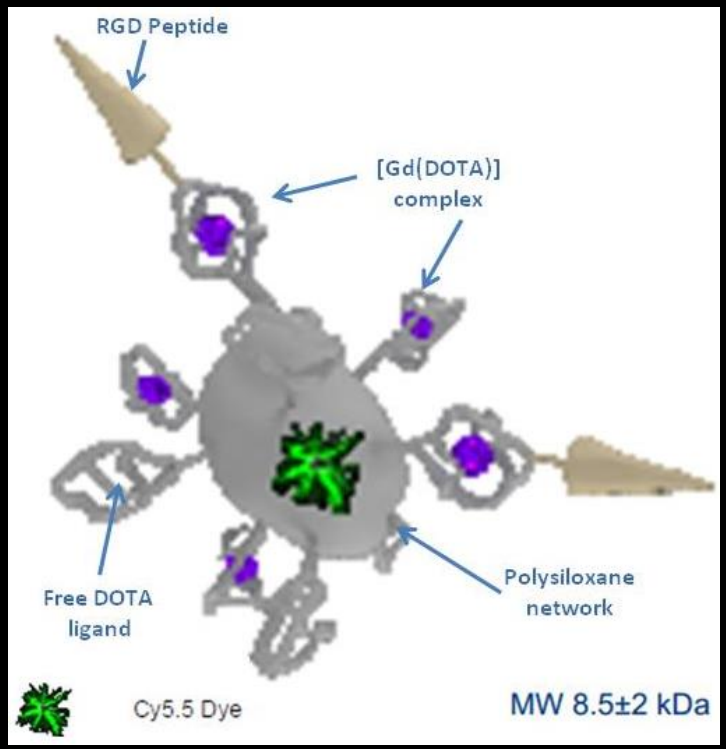
Theragnostic Nanoparticles

- (MRI-SPECT/PET- Radiotherapy)
- Ultrasmall size: (2-4 nm) – renal excretion
- DOTA (Gd) (MRI)

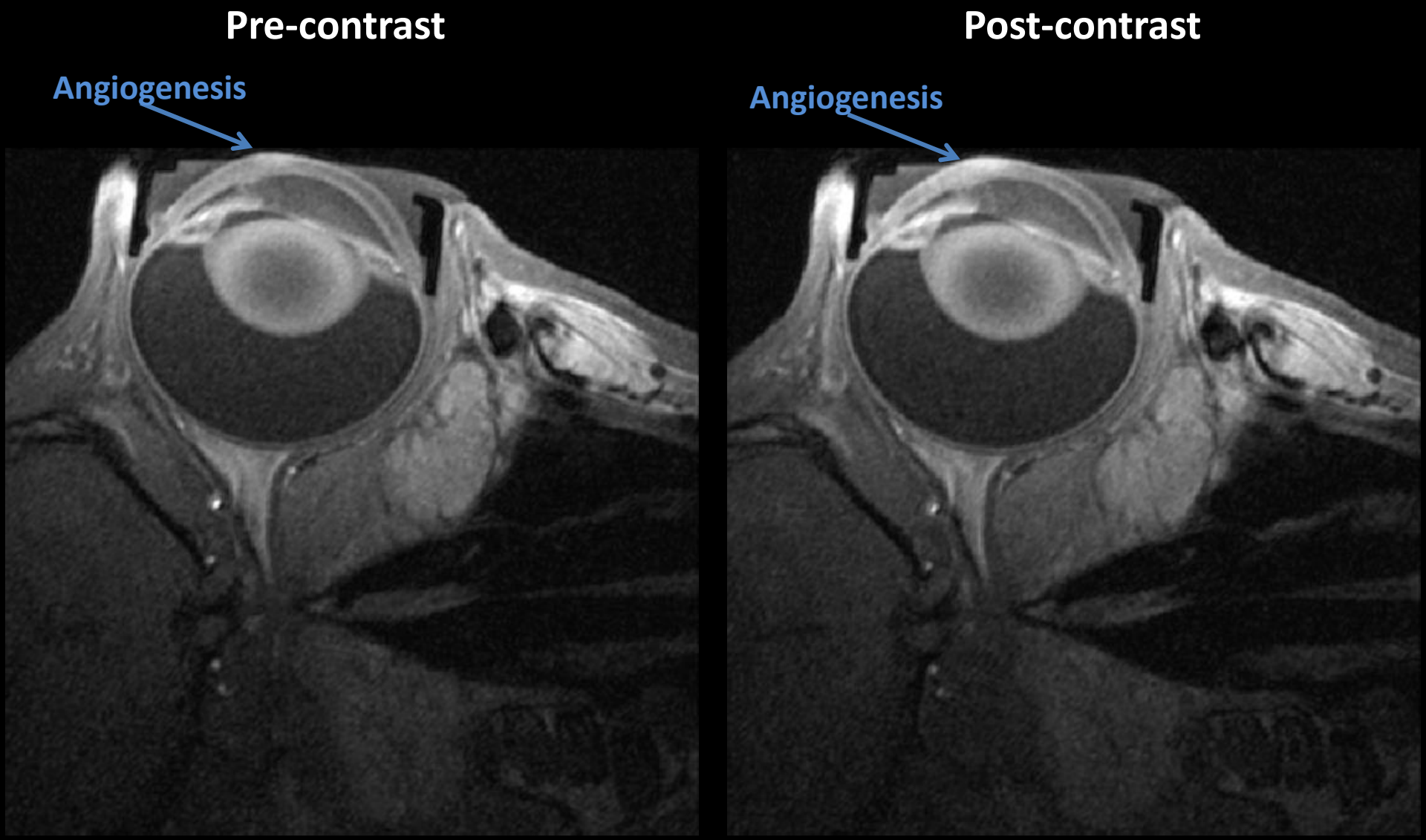
Gold(Au@DTDTPA-RGD)



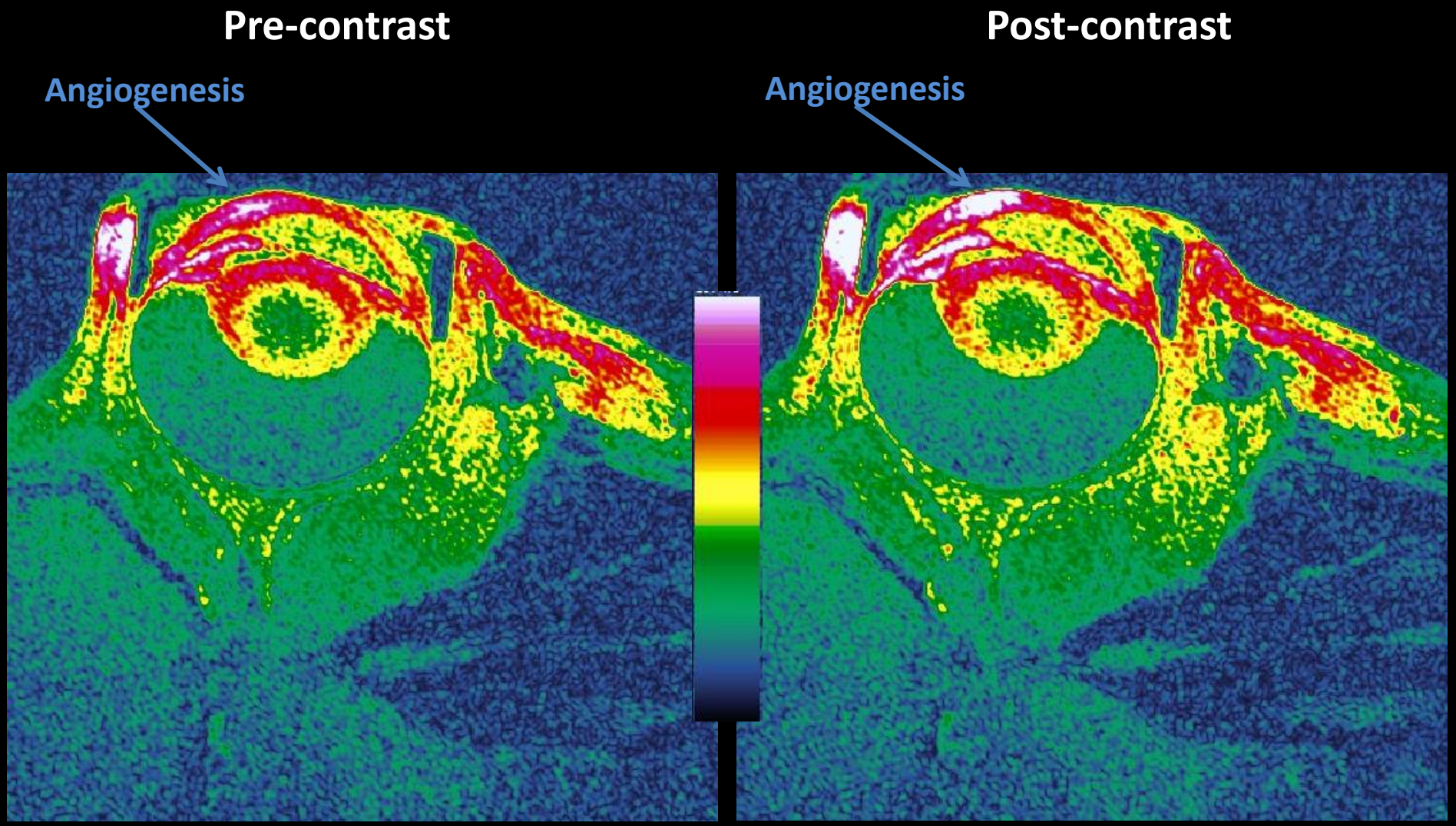
Polysiloxane composition AGuIX-[RGD]



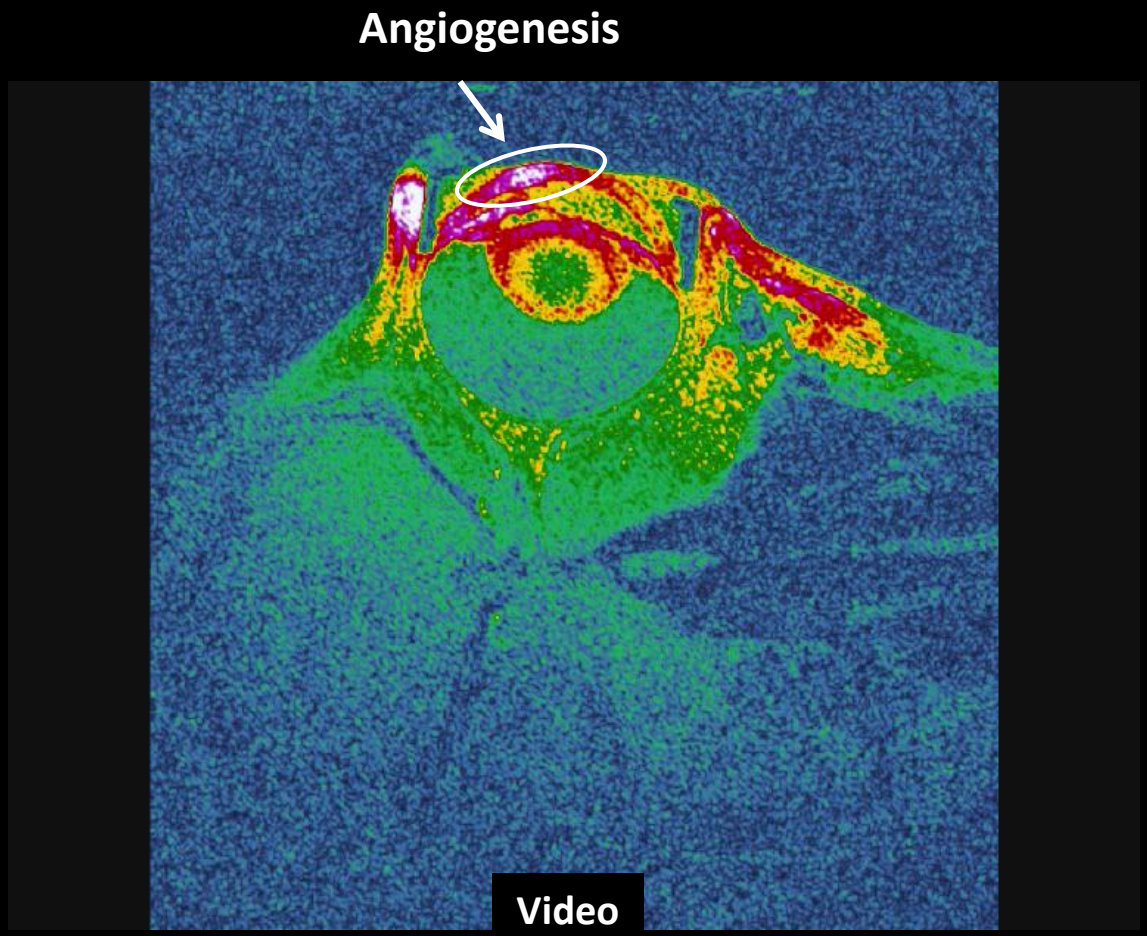
5ml iv. injection of polymer Nanoparticles (5mM AGUIX)



5ml iv. injection of Nanoparticles (5mM AGUIX)

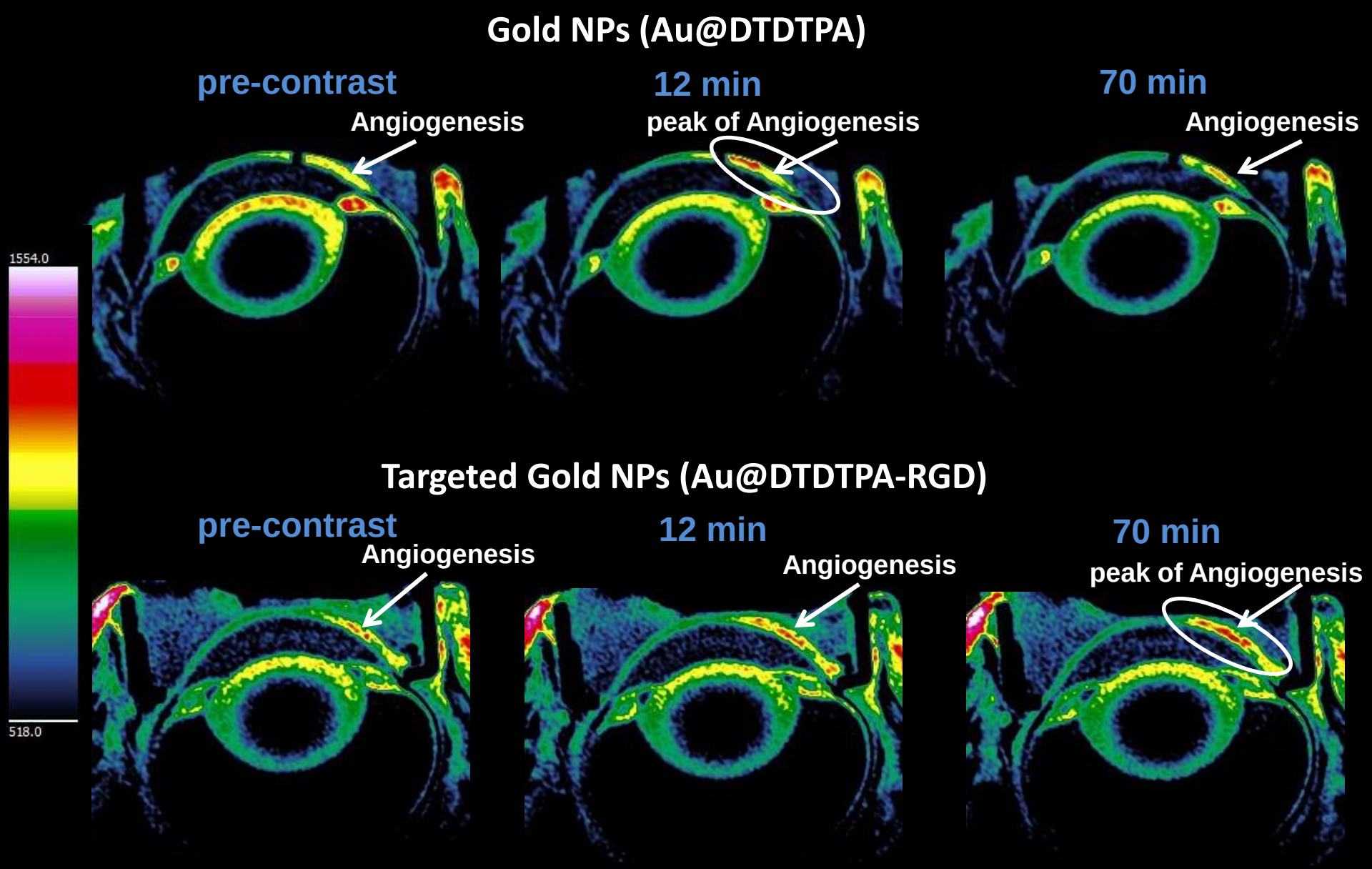


Dynamic MR imaging of 5ml iv. injection NPs (5mM AGUIX)



Snap duration: 0,19 min
Number of Snaps: 10
Total time: 1.9 min
Time of injection: 0.57 min

Preliminary Results of Corneal Angiogenesis using Gold NPs



Work in progress ….

- **MR-Eye Clinical Studies**

- **Multifunctional Gold NPs in MRI**
  - Imaging angiogenesis in different diseases
  - Radio-sensitize of Gold NPs using MRI system for tumor Therapy

- **MRI in ocular drug delivery**
  - Nanoparticles-Gd