Track 3
NanoMedicine
Session 2

1

Magnetic vectoring for drug delivery to tumors: Past, present and is there a future?

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- Hari S Sharma Uppsala University, Sweden
- Nanodrug delivery of a multimodal novel drug Cerebrolysin reduces engineered nanoparticles induced aggravation of heat stroke induced ubiquitin expression and brain pathology
-
- Jerzy Leszek Wroclaw Medical University, Poland
- Early detection and treatment of Alzheimer's disease--Nanotechnology as a tool
-
- Candan Tamerler University of Kansas, USA
- Tunable self-nanopatterned fluorescence proteins on metallic surfaces
-
- Anna Salvaı University of Groningen, The Netherlands
- Nanoparticle interactions with cells for targeting nanomedicines and potential impact of nanomaterials
-
- Wassana Yantasee Oregon Health and Science University, USA
- Bioreducible cross-linked polymer coated mesoporous silica nanoparticles for targeted delivery of siRNA and chemotherapeutics to HER2+ breast cancer

- Viya Fedoseyeva Russian Academy of Sciences, Russia
- Types of self-assembling of lengthy Intron RNA presented in the regions of homologue chromosomes somatic pairing
-
- Niren Murthy University of California at Berkeley, USA
- In vivo delivery of transcription factors with chemically modified oligonucleotides

- Ebru Basaran Anadolu University, Turkey
- Ocular application of dirithromycin with chitosan based polymeric nanoparticles
-
- Evrim Yenilmez Anadolu University, Turkey
- Formulation and characterization of dirithromycin nanoparticles for topical treatment
-
- Sree Harsha King Faisal University, Saudi Arabia
- Optimization of particles size for lung specific drug delivery by way of microspheres

- Manuel Fuentes University of Salamanca-CSIC, Spain
- Functional Proteomics for Biomarker and Drug Discovery
-
- Hussein Ammar National Research Center, Egypt
- New trends in site-specific drug delivery
-
- ArI Goel Amity University, India
- Green Nanotechnology
-
- Archana M Raichur Toyo University, Japan
- Strategist PLGA nano-capsules to deliver siRNA for inhibition of carcinoma and neuroblastoma cell lines by knockdown of proto-oncogene
-
- Lamees Nayef McGill University, Canada
- Testing the efficiency of a hybrid nanoparticulate drug delivery system for use in bone regeneration with distraction osteogenesis

EPR (Enhanced Permeability and Retention) Effect

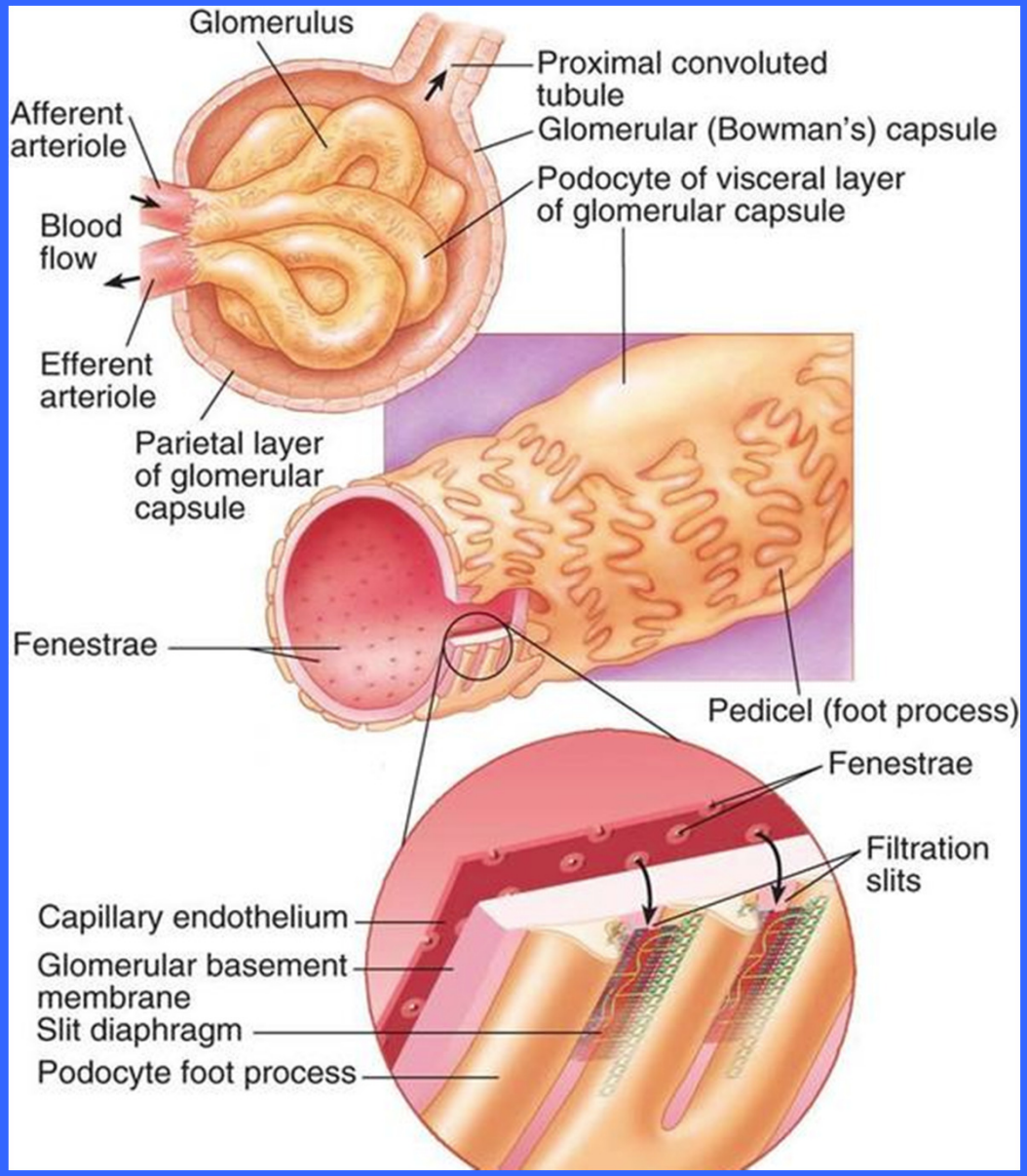
Matsumura, Y., and Maeda, H. (1986) A new concept for macromolecular therapeutics in cancer chemotherapy: Mechanism of tumoritropic accumulation of proteins and the antitumor agent SMANCS. *Cancer Res. 46*, 6387–6392.

- Demonstrated advantages in uptake/retention of macromolecules vs. small molecules/free drugs in tumor vs. normal tissues.
- Due to typically chaotic neovascularization of tumors and resultant architectural defects, tumor vasculature is hyperpermeable to macromolecules compared to normal vasculature.
- The lymphatic system is also defective or even essentially nonexistent in tumor tissue, causing delayed egress/increased retention of macromolecules/fluid.
- Combined with greater interstitial volume of tumor compared to normal tissue, in totality, typically increased uptake/retention of macromolecules by tumors.

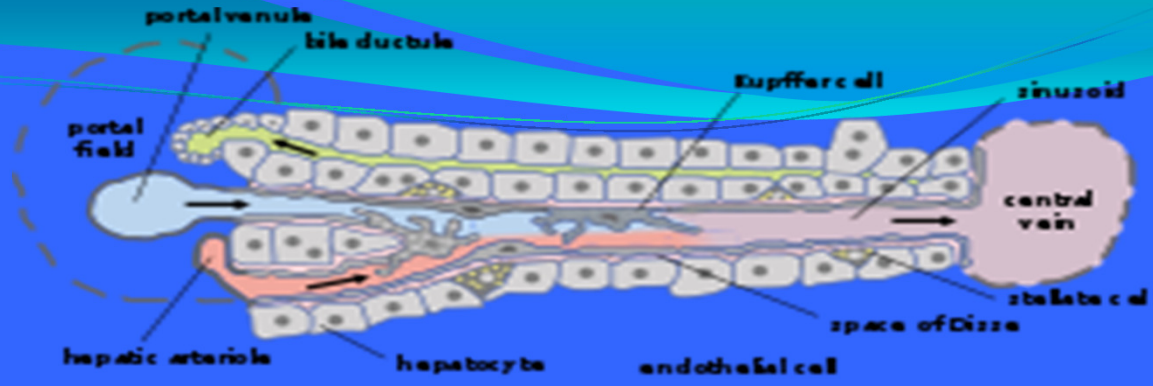
Barriers to Successful NP Extravasation into Tumors

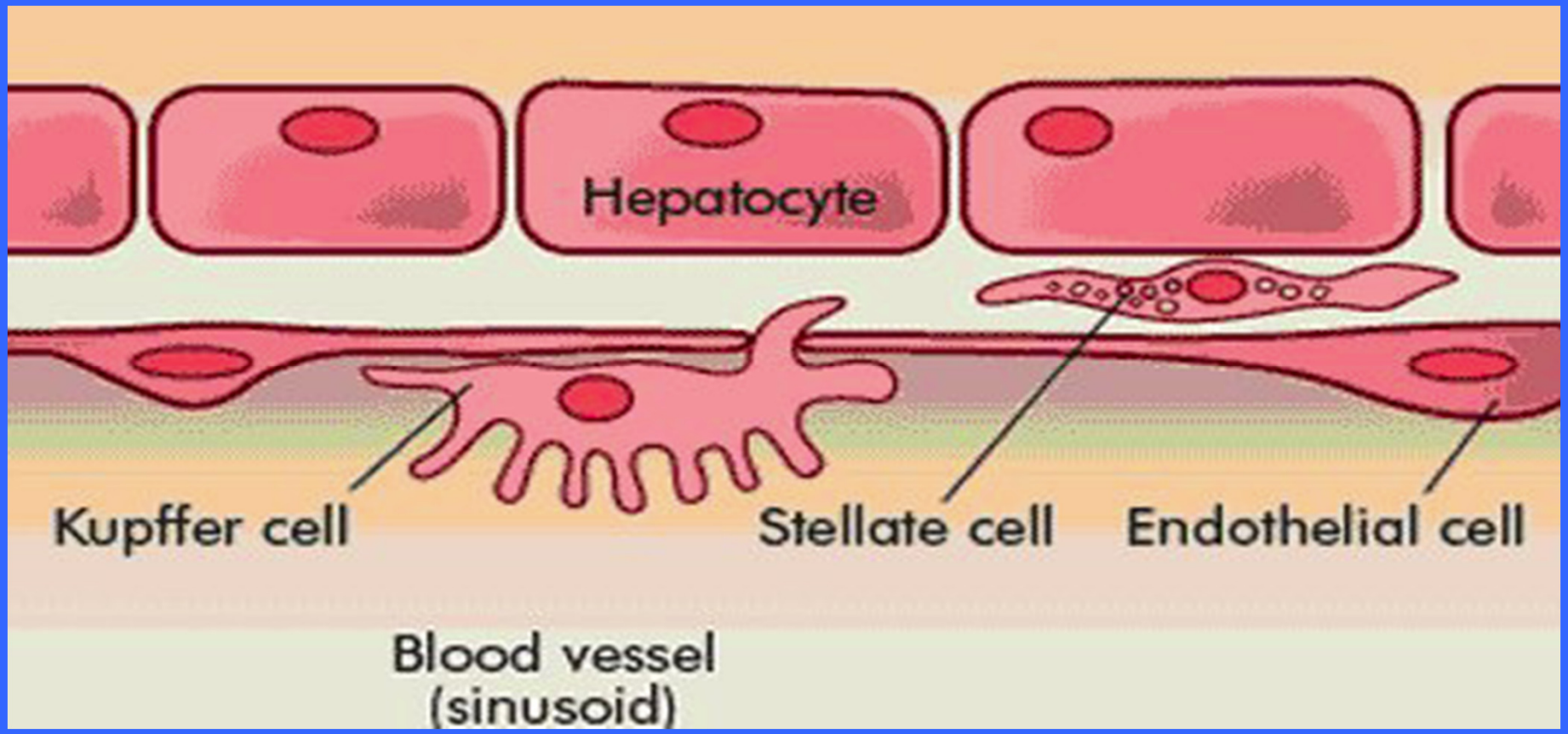
- Renal filtration
- Clearance by mononuclear phagocytes in liver (Kupffer cells), spleen, lung
- Transport from plasma into tumor interstitial fluid (e.g., gaps, fenestrations, among endothelial cells lining vessel; mural cells/pericytes)
- Distribution within tumor interstitial fluid (e.g., gradient of interstitial pressure, tumor ECM)

Renal Clearance



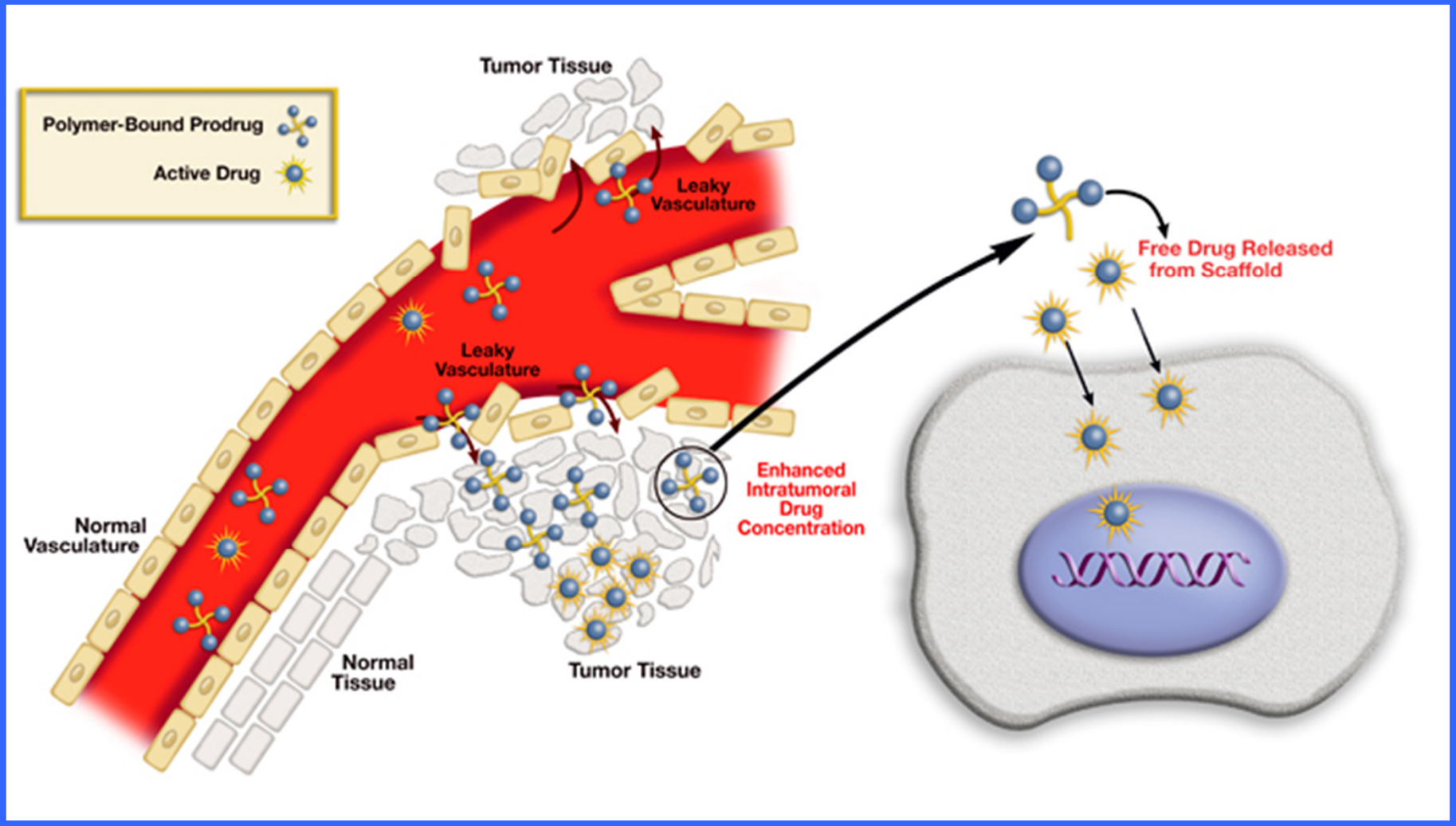
Hepatic Clearance (MPS)





NP Extravasation and Drug Payload Delivery

(largely diffusion controlled)



Early Clinical Experience

Lubbe et al. in Germany reported in 1996 Phase I clinical trial results with magnetic targeting of Epirubicin-loaded magnetite NP in 14 patients.

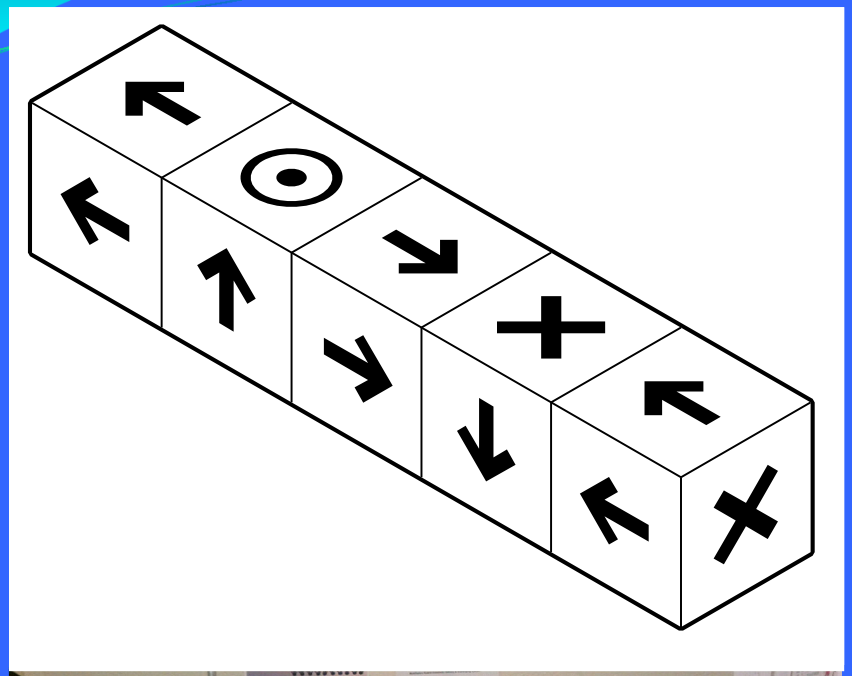
Key observations:

- With magnetic targeting, systemic drug side effects and drug plasma concentrations were reduced.
- Macroscopic and slowly reversible skin discoloration due to NPs, corresponding to boundary of over-laying magnets on superficial tumors.
- NP accumulation verified by histological techniques
- MRI also provided evidence of accumulation/extravasation

Thus, predictions of EPR effect were validated in humans.

The Challenge: to extend beyond current capability of magnetic localization only to superficial tumors to visceral/deeper sites

Superficial	Visceral
Locally Advanced Breast	Pancreatic
Melanoma/Sarcoma	ColoRectal
	Focal Recurrent Ovarian
To depths of up to several cm	To depths beyond several cm
Gradient created by one magnet/array	Gradient created by multiple magnets/arrays
Gradient on axis orthogonal to magnet face	Gradient nadir focused on tumor

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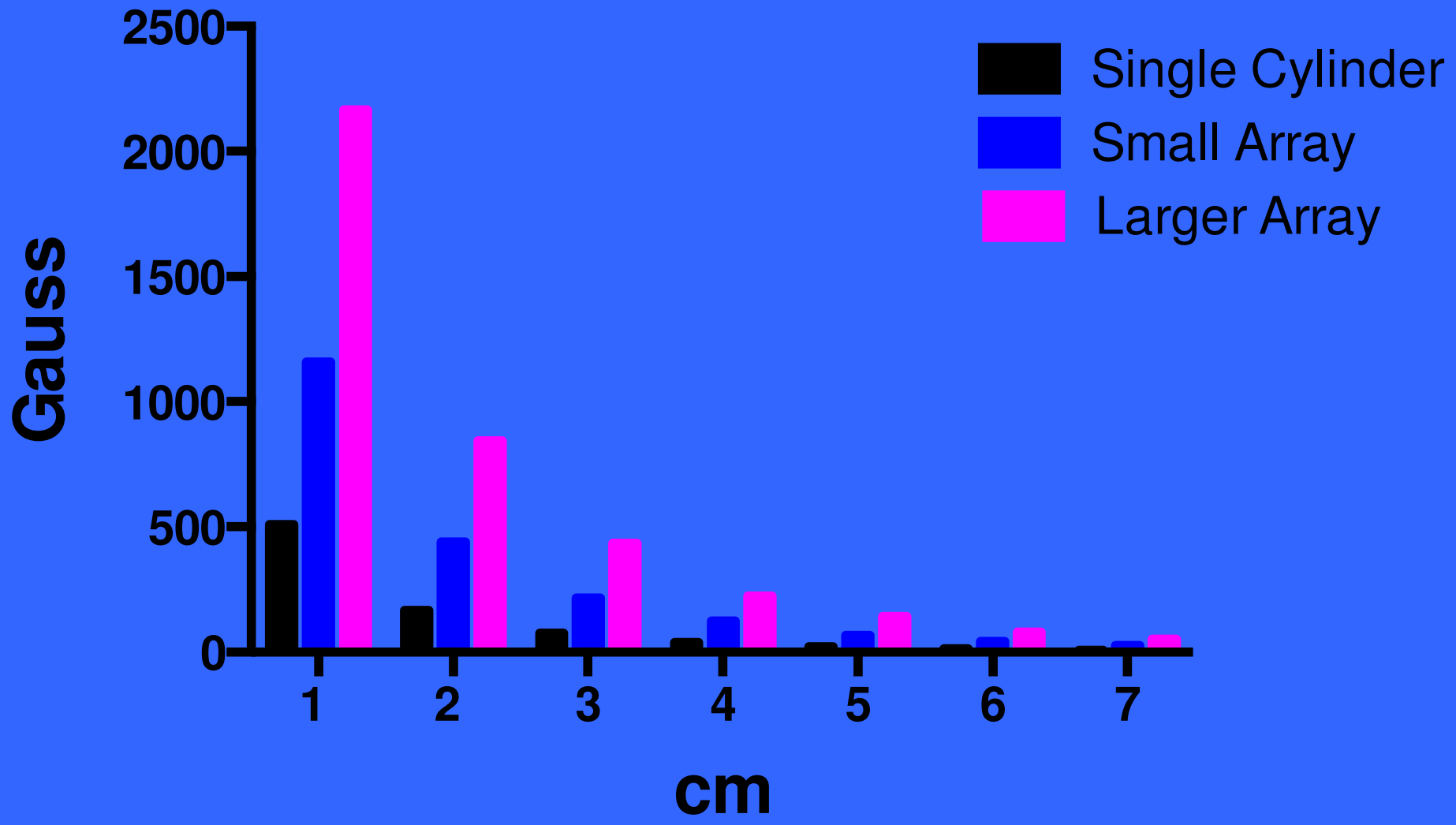
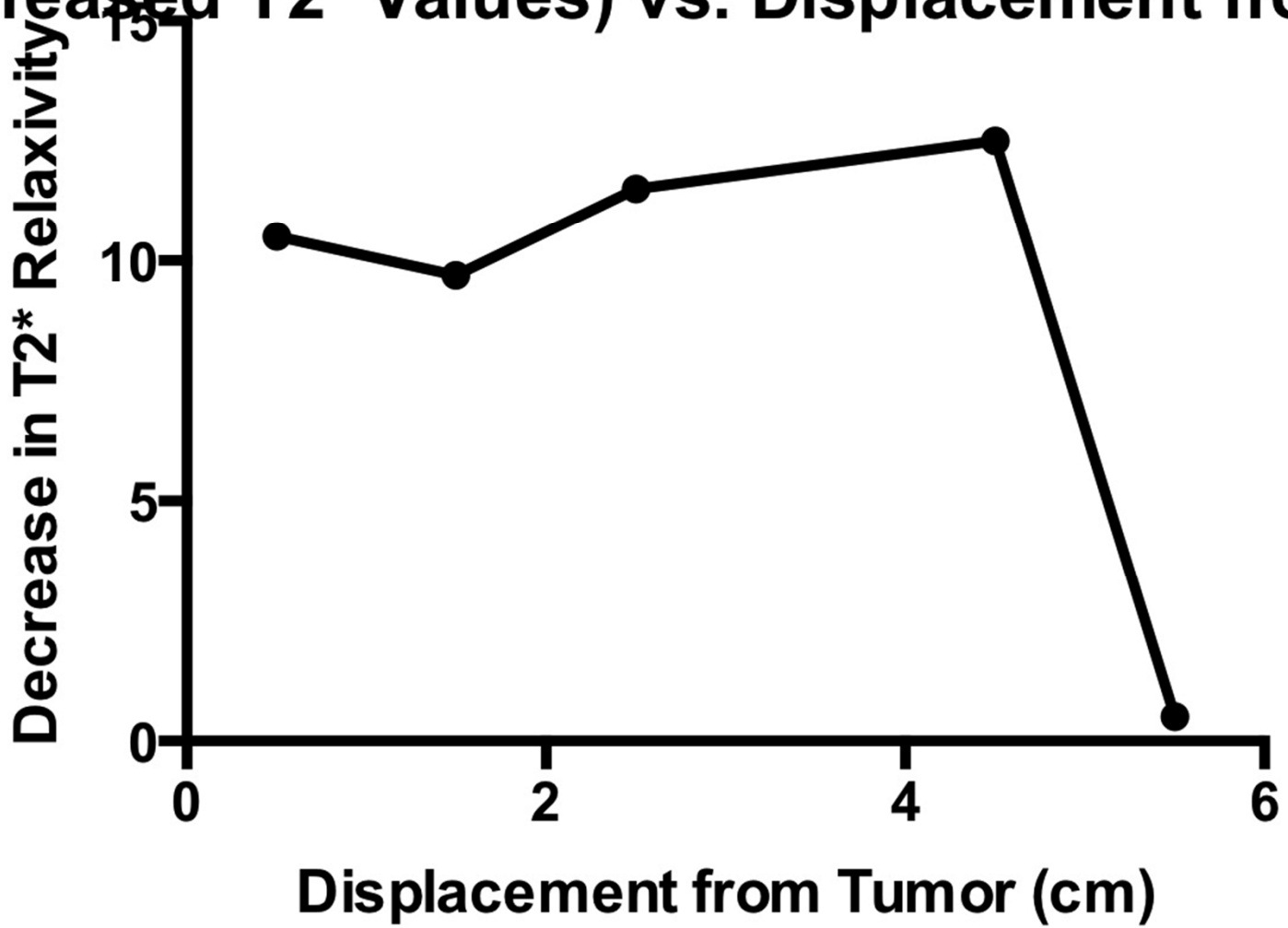
- 120.4

Gauss Values vs. Displacement

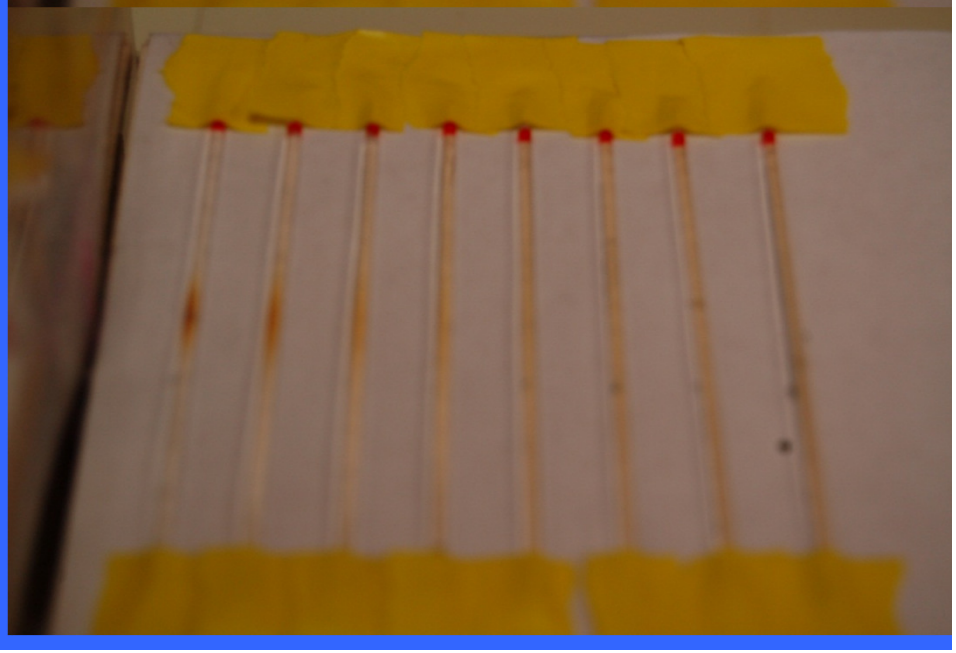


Smaller Array-Effects on MNP Accumulation (Decreased T2* Values) vs. Displacement from Tumor



Small array distance vs. T2*

Large array



Large array distance vs. T2*

summary

Thank You!

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