

How to Perform Dynamic Contrast Enhanced (DCE) MRI

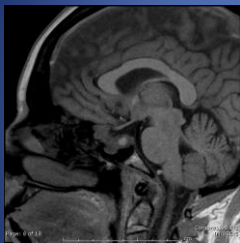
Chen Lin, PhD DABR
 Indiana University School of Medicine
 & Clarian Health Partners

Disclosure

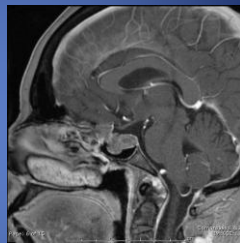
- Research funding provided by Siemens Healthcare

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Contrast Enhanced MRI Studies



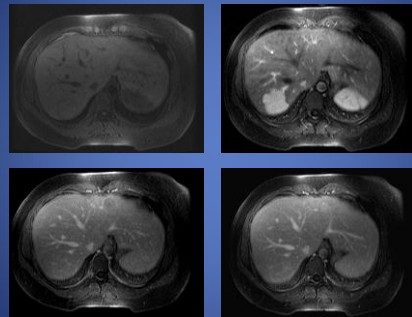
Pre-Contrast T1 Flash @ 3T



Post-Contrast T1 Flash @ 3T

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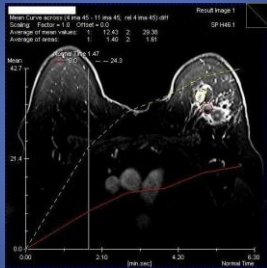
Hepatocellular Adenoma



4 time point (1 pre and 3 post) @ 30 sec – 5 min / time point

Courtesy of Faith Akisk @ IUSM

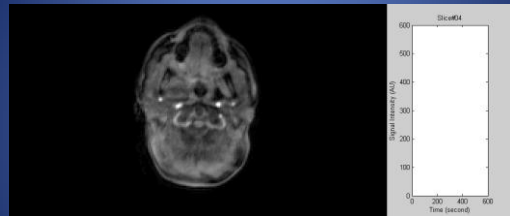
Dynamic Breast MRI



6 time points (1 Pre and 5 post) @ 60 – 90 sec / time pt

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DCE MRI of Neuro Fibromatosis



100 – 200 time point (10 – 30 pre) @ 2 – 10 sec / time point

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Courtesy of Guixie Bu @ IUSM

DCE MRI for Perfusion Quantification

- Tissue Blood Perfusion
- Measuring perfusion with MRI
- T1w GRE signal and Contrast Concentration
- DCE MRI Acquisition
- DCE MRI Post-processing
- Clinical applications of DCE MRI.
- Safety Issues related gadolinium based contrast agent

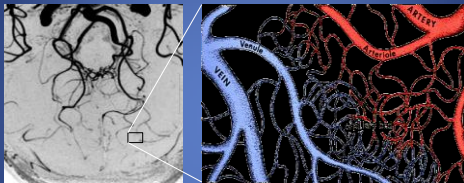
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MR Perfusion Imaging Methods

- Dynamic Susceptibility Contrast (DSC) MRI Perfusion
 - GRE-EPI (T2* weighted)
- Dynamic Contrast Enhanced (DCE) MRI Perfusion
 - Spoiled Fast Gradient Echo (T1 Weighted)
- *Arterial Spin Labeling*
- *Intra Voxel Incoherence Motion*

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Blood Perfusion



- Deliver oxygen and nutrients to the cells
- Affected by pathological and physiological conditions, such as tumor angio-genesis, stroke and infarct, vascular wall changes.

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Perfusion through Capillary System

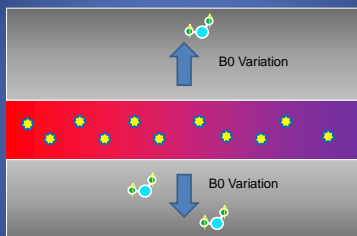


- Blood Flow (ml of blood / gram of tissue / sec)
- Blood Volume (ml of blood / gram of tissue)
- Mean Transit Time (MTT) (sec)

$$\text{CBF} = \text{CBV} / \text{MTT}$$

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T2* Effect from Gd in Blood Vessel



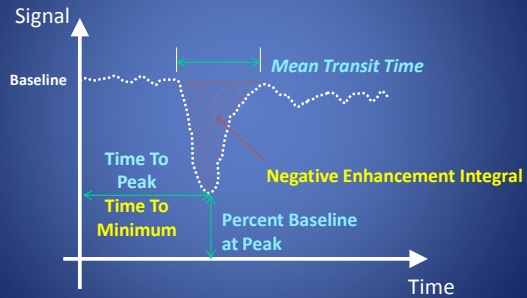
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Typical DSC Brain Perfusion Protocols

- Single shot GRE-EPI or SE-EPI
- TE = 30 – 60 ms (GRE-EPI) or 50 – 80 ms (SE-EPI)
- TR = min. (< 2 sec depends on number of slices)
- TA = 90 - 120 sec. or ~ 100 time points
- Contrast dose = 0.1 – 0.2 mmol/kg
- Injection rate: 3 – 5 ml/sec with 20 ml saline flush.

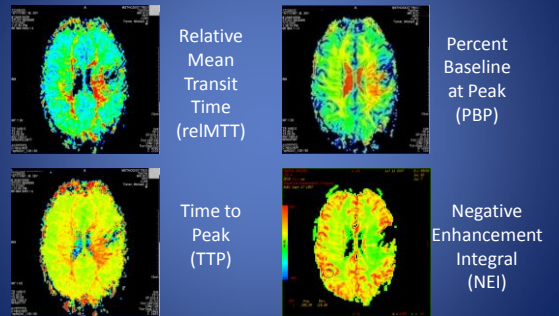
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DSC Perfusion Imaging



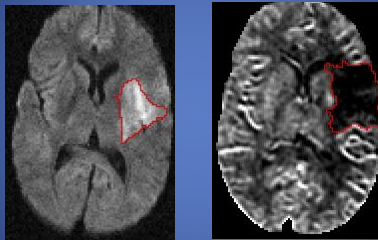
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DSC Perfusion Maps



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DWI / PWI Mismatch in Stroke



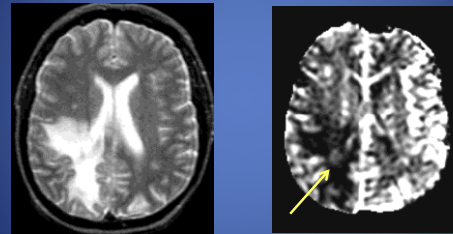
DWI @ 4hr

rCBV @ 4hr

Courtesy of Sorensen @ MGH

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Tumor versus Radiation Necrosis

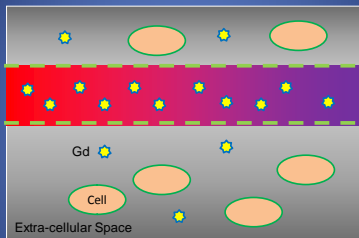


T2w

rCBV

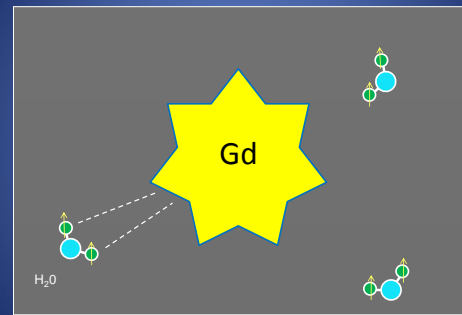
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Leakage and Extra-cellular Space



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T1 Effect from Gd in the Extra-cellular Space



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DCE Perfusion Imaging

1. Contrast Injection Protocols
2. DCE MRI Acquisition Protocols
3. DCE MRI Quantification
 1. Arterial Input Function
 2. Relationship between T1 value and Contrast Concentration
 3. Pharmacokinetic Modeling

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1. Contrast Injection

- Type of Contrast
- Dose = 0.05-0.1 mmol/kg
- Injection rate: 3-5 ml/sec with 15-20 ml saline flush.
- Injection timing: allow 10 – 30 frames before contrast arrival.

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2. DCE MRI Acquisition

- Spoiled 2D or 3D GRE sequence (SPGR or FLASH)
- TR/TE/FA = min. /min. / 10 – 30 deg
- Matrix: Balance between spatial and temporal res.
- Parallel Imaging, partial Fourier and other acceleration techniques
- Imaging plane/slab: Depending geometry of the lesion, the location, flow direction and velocity of the feeding artery
- Motion compensation and image registration
- Fat Suppression (See Spring 2010 seminar)

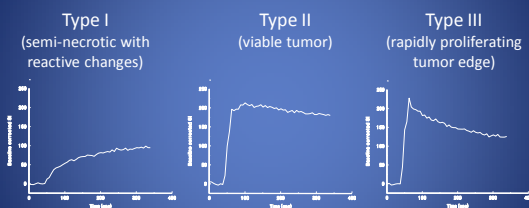
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DCE MRI Acquisition (Cont'd)

- Acquisition window :
 - Long enough to capture the contrast uptake and stabilization in tissue. (5 – 10 min)
 - Blood volume and blood flow short.
 - transfer constant from intra-vasculature space to tissue long.
 - transfer constant rate from tissue back to intra-vasculature space longer.
 - Lower frame rate when reaching stabilization.
 - Introducing delay between acquisitions.
 - Reduce the amount of data

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DCE-MRI Signal Time Curve



(Taylor and Reddick, Adv Drug Del Rev, 2000)

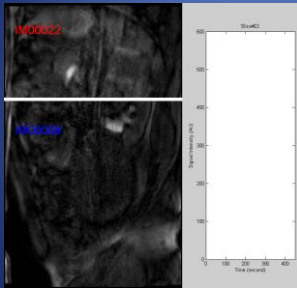
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3. DCE-MRI Quantification

- Qualitative - shape of signal intensity (SI) data curve
- Semi-quantitative - indices that describe one or more parts of signal intensity curves
 - Uptake slope, max amplitude, washout rate or area under curve.
- True quantitative - indices from contrast medium concentration changes using pharmacokinetic modelling

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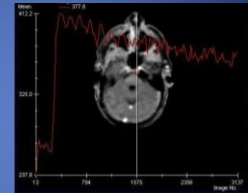
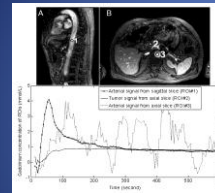
3.1 Arterial Input Function (AIF)



- Signal intensity change over time in the feeding artery.
- No necessary in the same slice.
- Can be averaged over multiple pixels and slices to reduce noise.

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Selection of Vessel/ROI for AIF

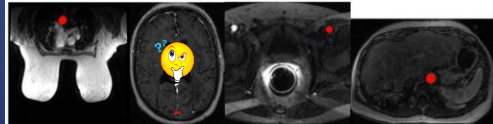


- In-flow effect (TOF)
- T2* effect due to high Gd concentration
- Time delay
- Partial volume effect

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Automatic Search for AIF

- Global search within the imaging volume
 - Select pixels based peak signal intensity, uptake slope and geometry analysis (has a shape like a vessel in 3D)

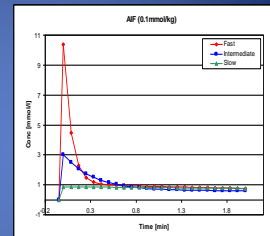


J. Chen et al Med Image Comput Assist Interv. 2008; 11(Pt 1): 594–601

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Empirical Modeling of AIF

- bi-exponential function
- 3 different modes (fast, intermediate, slow).
- Scale with contrast dose and body weight



$$C_p(t) = d * (a_1 * \exp(-m_1 * t) + a_2 * \exp(-m_2 * t))$$

$$d = \text{mol} * v / \text{bw}$$

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3.2 Estimating Contrast Concentration

$$R_1(t) = R_1(0) + C(t) * R_{Gd}$$

- $R_1(t)$: Relaxation rate during dynamic acquisition.
- $R_1(0)$: Relaxation rate at baseline before contrast arrival.
- R_{Gd} : Relaxivity of the contrast agent (a know value)
 - $4.5 \text{mM}^{-1} \text{sec}^{-1}$ for Magnevist at 3T
- $C(t)$: Contrast concentration time curve.

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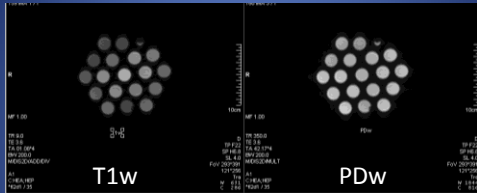
Measuring $R_1(t)$

$$R_1(t) = \frac{1}{TR} \ln \left(\frac{1 - \left[\frac{S_{T1w}(t)}{S_{PDw}} \right] \cos(\alpha)}{1 - \left[\frac{S_{T1w}(t)}{S_{PDw}} \right]} \right)$$

$S_{T1w}(t)$: Signal intensity of T1w images at time, t.

S_{PDw} : Signal intensity of PDw images at baseline.

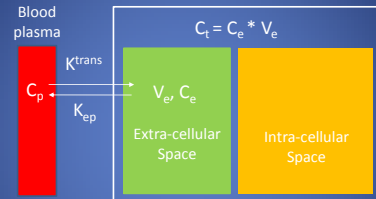
Phantom Calibration Approach



- Estimating $C(t)$ by looking up the Gd concentration in the vial producing the same $S_{T1w}(t)/S_{PDw}$
- Must use the same contrast, field strength, $T1w$ and PDw protocols to scan phantoms

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3.3 Pharmacokinetic Modelling (Tofts Model)



- K^{trans} : transfer constant (Vessel Permeability)
- K_{ep} : reflux constant
- V_e : extra-vascular, extra-cellular volume fraction (Cellular Density)

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Fitting the Tofts Model

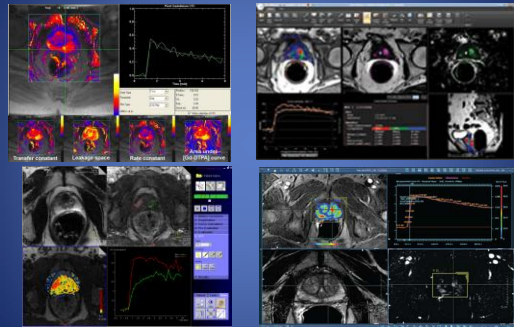
$$\frac{dC_i(t)}{dt} = K^{trans} C_p(t) - k_{ep} C_i(t)$$

$$k_{ep} = \frac{K^{trans}}{V_e}$$

- $C_p(t)$: Blood contrast concentration, arterial input function (AIF).
- Perfusion result: K^{trans} , K_{ep} and V_e

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Software Tools for DCE MRI Analysis



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Quantitative analysis with pharmacokinetic modelling

- Advantages
 - Whole curve shape is analysed
 - Produce biologically relevant physiological parameters
 - Independent of imaging protocols, ...
 - Enables valid comparisons of serial measurements and data exchange between different imaging centres
- Disadvantages
 - Data acquisition and analysis is more complex
 - Offline processing is required
 - Models may not fit the data observed

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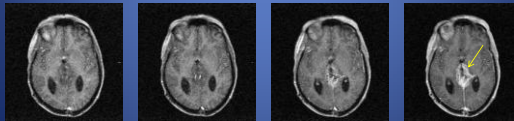
Clinical Applications of DCE MRI

- Cancer / Tumor
 - Volumetric CT, FDG-PET and DCE-MRI have been identified as the most promising imaging techniques
 - Brain / Liver / Pancreas / Prostate
 - Accessing early treatment response prior to morphological changes
- Myocardium Ischemia
- Kidney Function (GFR)
- *Atherosclerotic plaque, ...*

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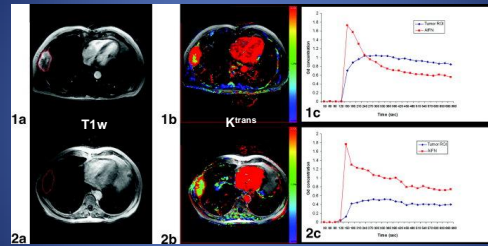
DCE Perfusion of Brain Tumor

- T1 weight spoiled fast gradient echo with Fat Sat
- TE = Min. (1-2ms); TR = Min. (4-5ms)
- FA = 30 – 35 deg
- Matrix = 128 x 128 x 24-32
- Measurements = 100 + baseline T1 measurements with variable flip angle.



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DCE Perfusion of Metastatic Melanoma

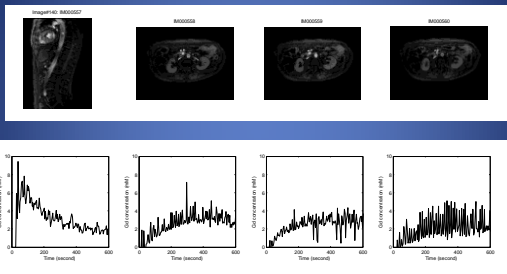


Bottom row: two weeks after Topotecan antiangiogenic therapy

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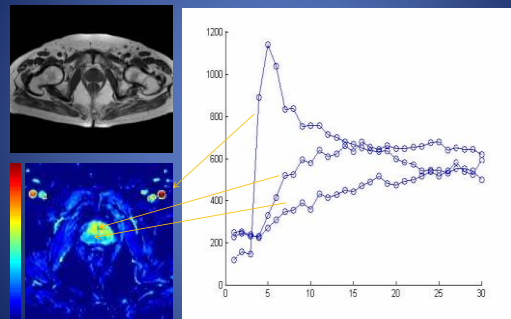
Barrett T. JMRI 2007 Aug;26(2):235-49

DCE Perfusion of Pancreatic Tumor



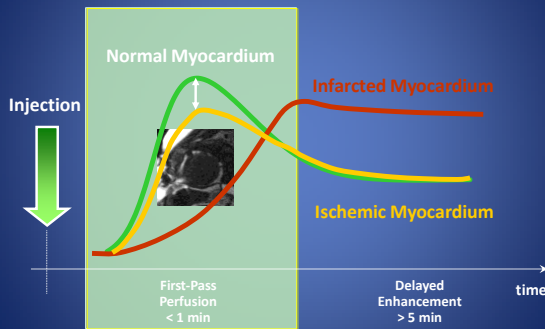
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DCE Perfusion of Prostate



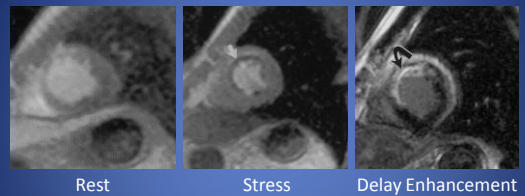
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Adenosine Stress Myocardial Perfusion



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Combine First-pass perfusion and Delay Enhancement

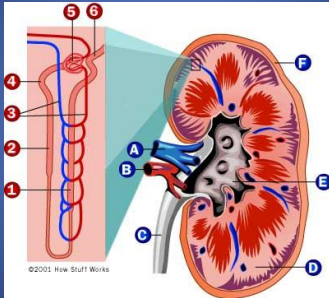


- Use Inversion recovery or Saturation recovery to improve T1 contrast.
- Use bSSFP for faster acquisition

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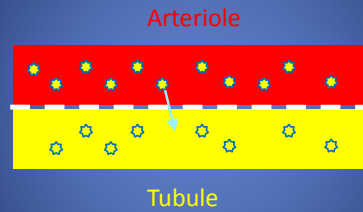
Chiu et al Radiology. 2003 Mar;226(3):717-22

DCE MRI of Kidney (MR Urography)



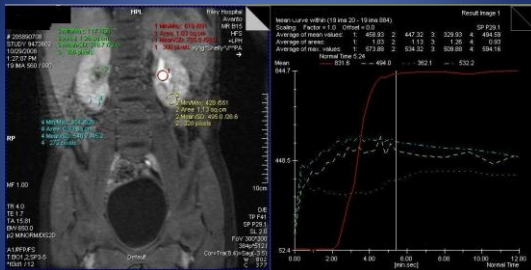
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Filtration in Glomerulus



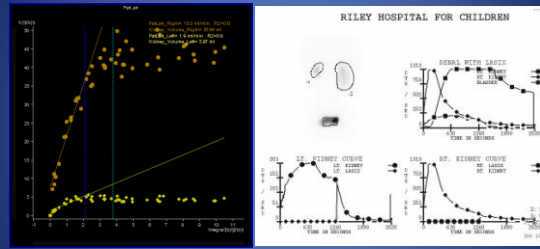
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DCE MRI of Kidney



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Estimation of Kidney Function



Contrast Enhanced MR Urography

Renal Scintigraphy (Tc^{99m})

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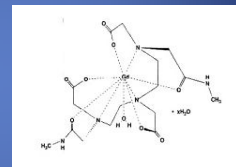
MR Contrast Agent Safety

- Contrast Reaction:
 - Headache (6.5%), Injection site coldness (3.6%), Injection site pain or burning (2.5%), and Nausea (1.9%).
 - Severe allergic reactions (0.01%)
- Contrast Toxicity & Contrast Induced Nephropathy (CIN)
- High Risk Groups:
 - Pregnancy/Breast Feeding
 - Previous Contrast Reaction
 - Renal Deficiency and slow clearance.

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Gadolinium-Based Contrast Agent (GBCA)

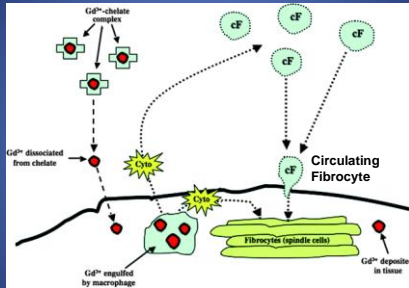
- Paramagnetic ion.
- Decreases relaxation times and, therefore, alters image contrast.
- Gd³⁺ is toxic in free state.
- Imbedded in a large molecule (Chelate)



Gadodiamide (Omniscan)

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Speculated Mechanism of NSF



Perazella, M. A. Clin J Am Soc Nephrol 2007;2:200-202

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FDA Approved GBMCA

Generic	Brand Name	Manufacture	FDA Approval	Market Share	NSF Cases*
Gadopentetate dimeglumine	Magnevist	Bayer	1988	~50% (70M Doses)	85
Gadodiamide	OmniScan	GE / Amersham	1993	35%	21
Gadoversetamide	OptiMARK	Covidien	1999	5%	6
Gadoteridol	ProHance	Bracco	1992	10%	1
Gadobenate dimeglumine	MultiHance		2004		
Gadoxetate	Eovist	Bayer	7/2008	?	?
Gadofosveset	Ablavar	Lantheus	12/2008	?	?

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* As of Jan 2007

Latest FDA Recommendations

- Not use three of the GBMCA drugs--Magnevist, Omniscan, and OptiMark--in patients with AKI or with chronic, severe kidney disease. These three GBMCA drugs are contraindicated in these patients.
- Screen patients prior to administration of a GBMCA to identify those with AKI or chronic, severe, kidney disease. These patients appear to be at highest risk for NSF.
- Use the clinical history to screen patients for features of AKI or risk factors for chronically reduced kidney function.

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Latest FDA Recommendations

- Features of AKI consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury, or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess kidney function in the setting of AKI.
- For patients at risk for chronically reduced kidney function (such as patients over age 60 years, patients with high blood pressure, or patients with diabetes), estimate the kidney function (GFR) through laboratory testing.

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Latest FDA Recommendations

- Avoid use of GBMCA in patients suspected or known to have impaired drug elimination unless the need for the diagnostic information is essential and not available with non-contrasted MRI or other alternative imaging modalities.
- Monitor for signs and symptoms of NSF after a GBMCA is administered to a patient suspected or known to have impaired elimination of the drug.
- Do not repeat administration of any GBMCA during a single imaging session.

<http://www.fda.gov/Drugs/DrugSafety/ucm223966.htm>
(9/9/2010)

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NSF Risk Factors

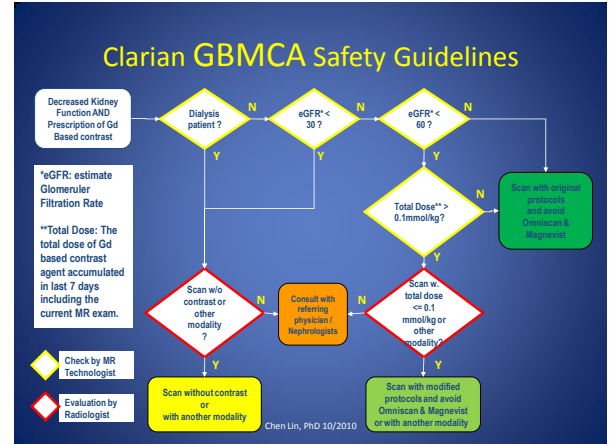
1. Type of contrast agent and dosage
2. Renal Insufficiency
 - Acute/Chronic
 - Accessed by clinical history, age
 - Measured with eGFR/Scr
3. Impaired drug elimination
4. Proinflammatory events (vascular endothelial dysfunction)

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NSF Remedies

- Avoid/minimize the use of Gd contrast agents in the risk population:
 - Patient screening
 - Use minimal dosage needed and avoid multiple injection in a short period of time.
 - Non-contrast enhanced MRI techniques
 - Other modalities
- Hemodialysis, Hydration?

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Thank You !

<http://www.indiana.edu/~mri/seminars/seminars.html>