

## **MEDICAL IMAGE COMPUTING (CAP 5937)**

### **LECTURE 4: Pre-Processing Medical Images (II)**

**Dr. Ulas Bagci**

HEC 221, Center for Research in Computer  
Vision (CRCV), University of Central Florida  
(UCF), Orlando, FL 32814.

[bagci@ucf.edu](mailto:bagci@ucf.edu) or [bagci@crcv.ucf.edu](mailto:bagci@crcv.ucf.edu)

# Outline

- Diffusion based Smoothing in Medical Scans
- Intensity inhomogeneity Correction in MRI

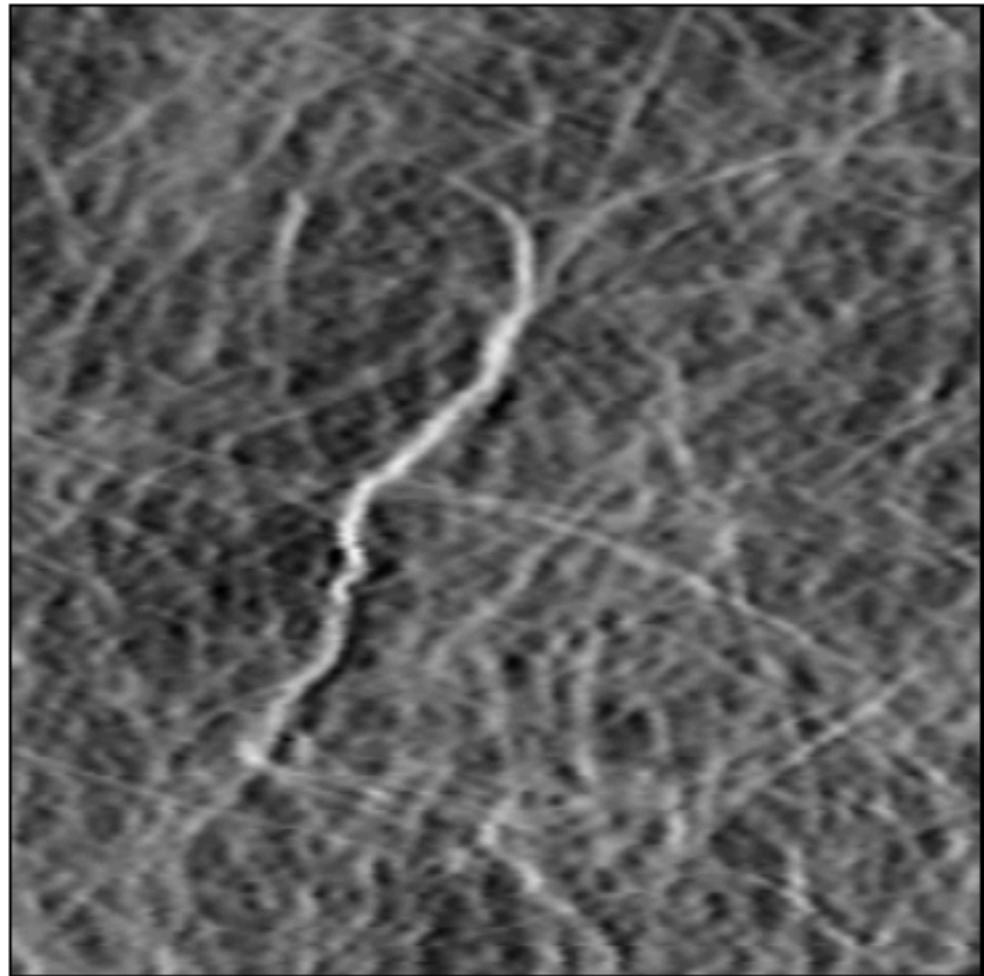
# Linear and Non-Linear Filtering (Smoothing)

## ***Linear approach:***

Treat every pixel with the exact same convolution.

## ***Non-Linear approach:***

Treat a pixel with varying intensity, depending on its neighborhood qualities.



Possible?

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- approximation  $\partial_t u = \nabla u$

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- if  $(x,y)$  is a part of an edge  $\rightarrow$  apply little smoothing
- Else  $\rightarrow$  apply full smoothing
- Assume,  $E$  is edge likelihood (telling you if you are in homogeneous or edge regions)
- CONTROLLING THE BLURRING (SMOOTHING)

$$g(\|E\|) = e^{-((\|E\|/k)^2)}$$

or

$$g(\|E\|) = \frac{1}{1 + \left(\frac{\|E\|}{k}\right)^2}$$

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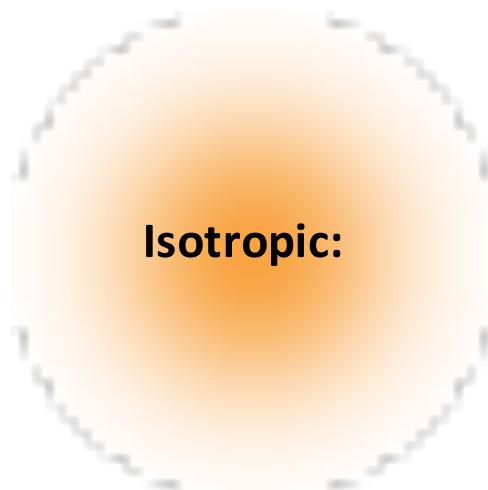
$$[I(\mathbf{x})]_{t+1} = \left[ I(\mathbf{x}) + (\Delta T) \sum_{d=1}^{\Gamma} c_d(\mathbf{x}) \nabla I_d(\mathbf{x}) \right]_t,$$

$d=1, \dots$  direction

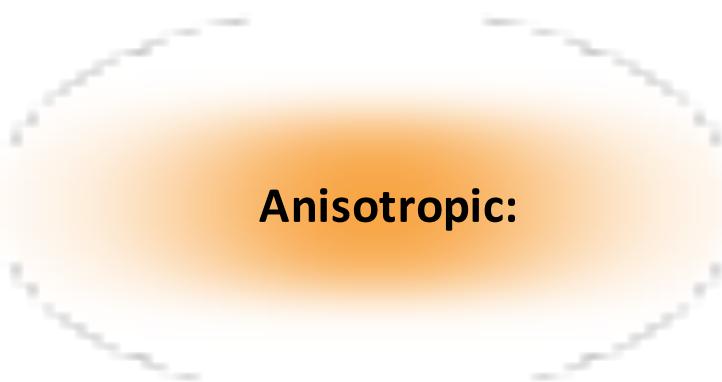
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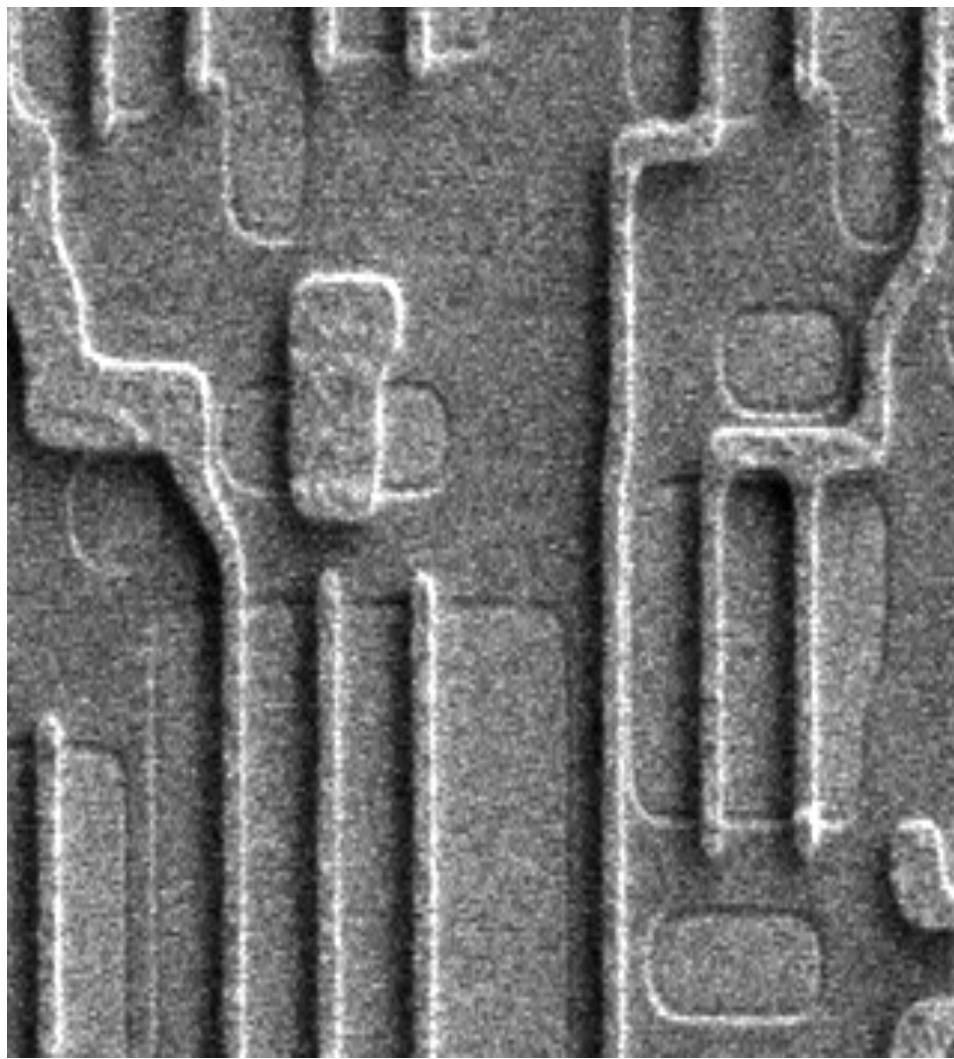


Isotropic:



Anisotropic:

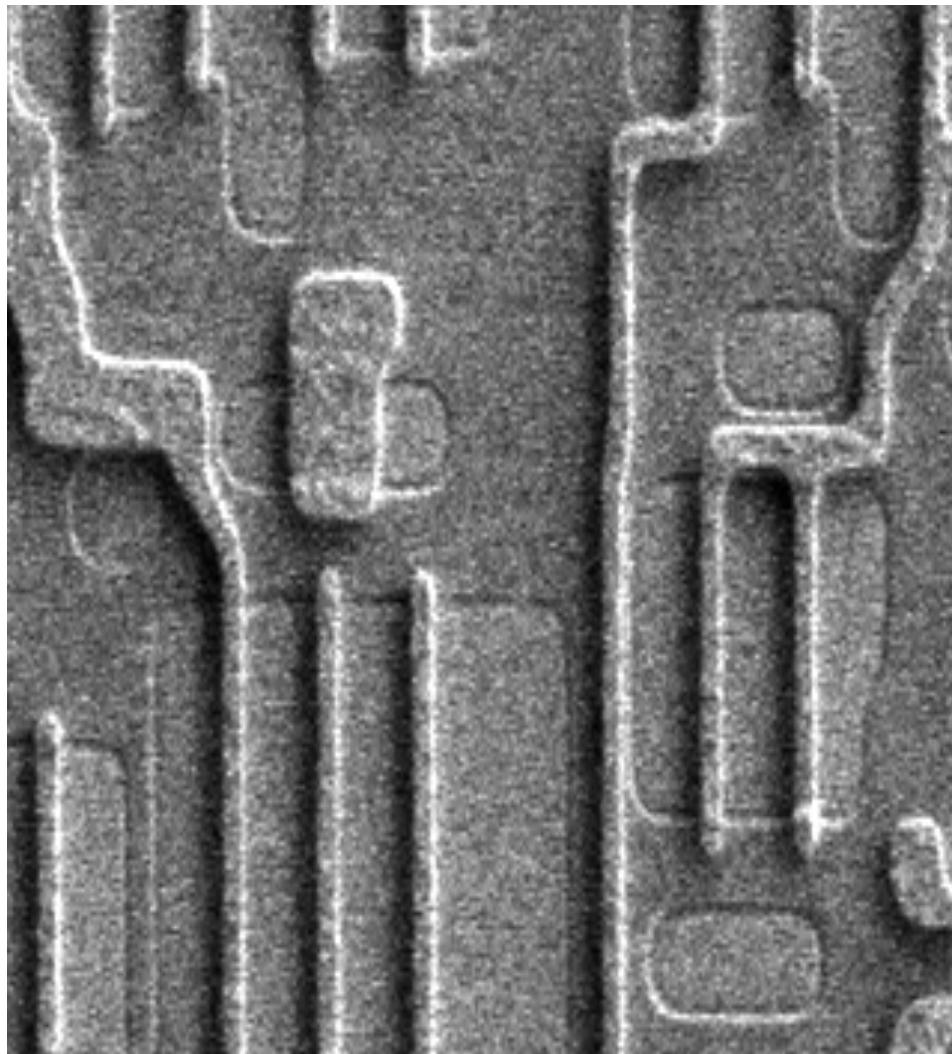
Original



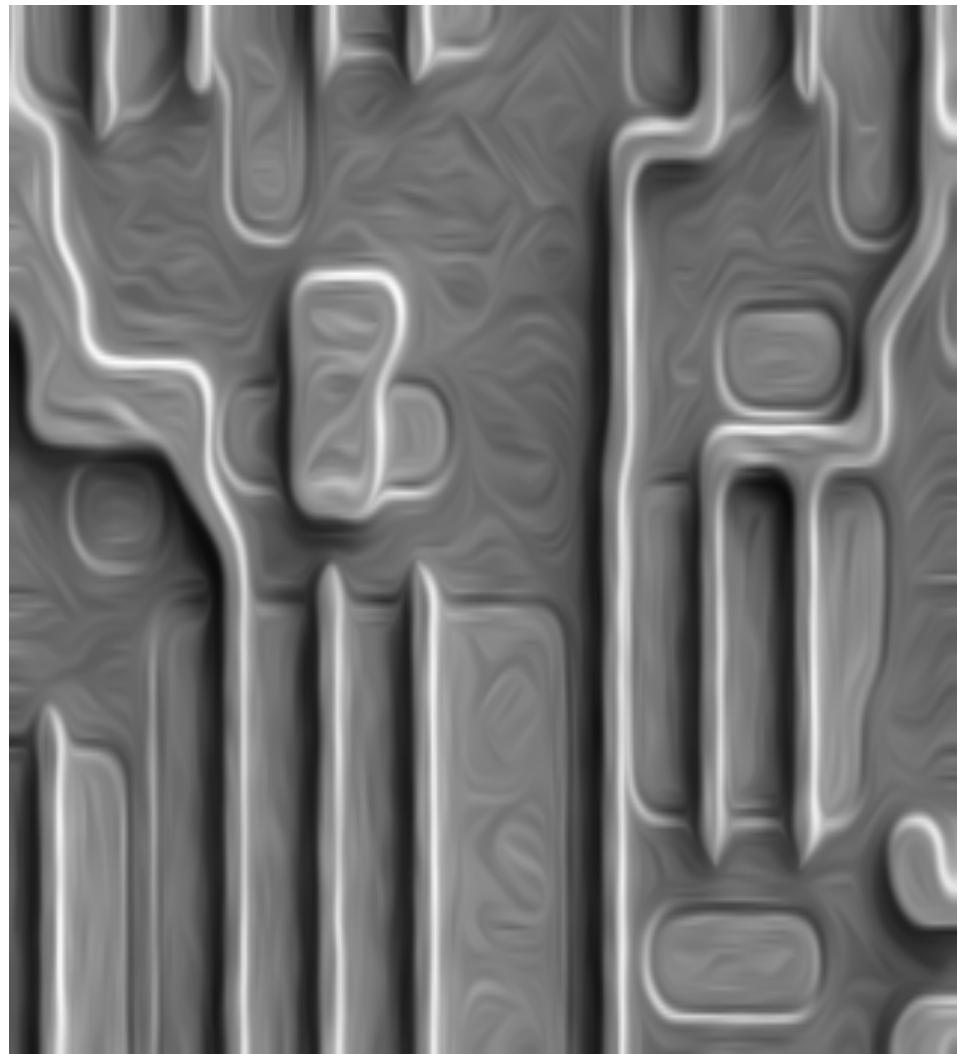
Linear isotropic diffusion  
(simple Gaussian)



Original

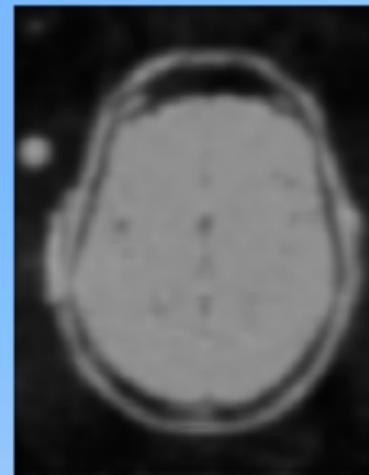


Non-linear anisotropic diffusion

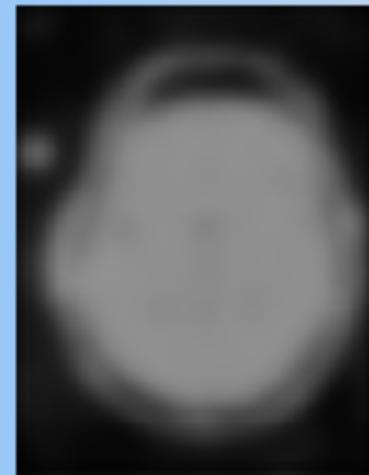




Linear  
diffusion



$t=4$

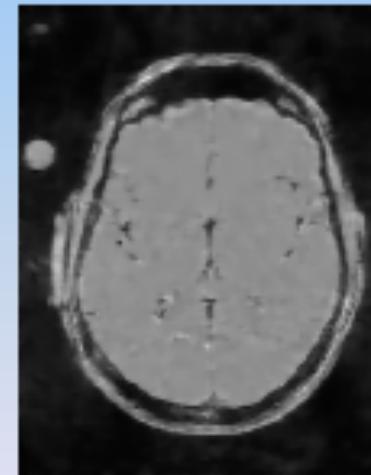


$t=20$

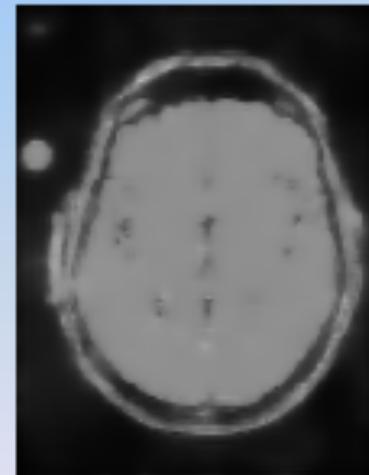


$t=40$

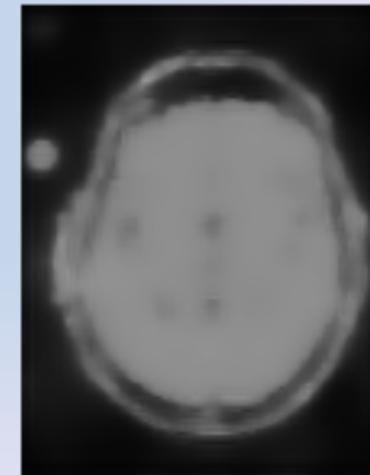
Nonlinear  
diffusion



$t=4$



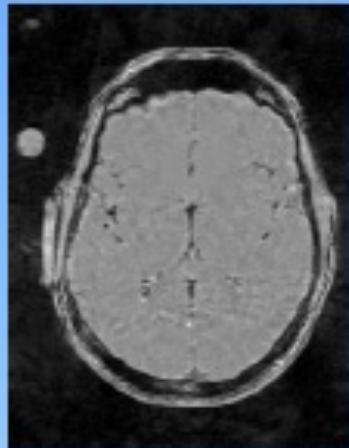
$t=20$



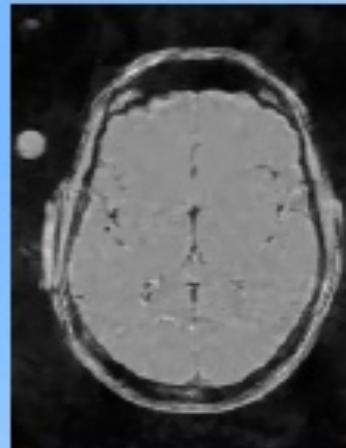
$t=40$



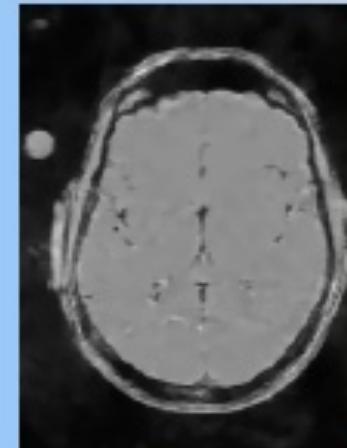
## Non-linear Diffusion



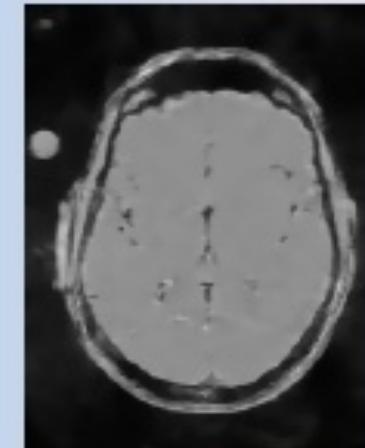
$t=0$



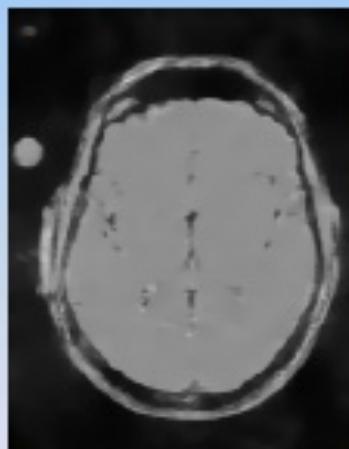
$t=4$



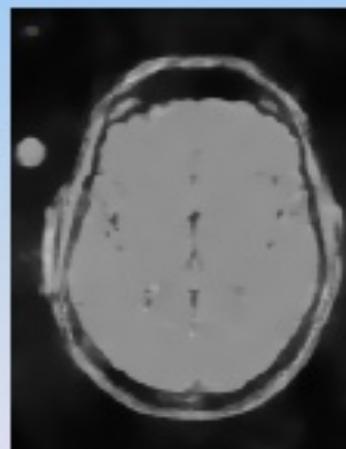
$t=8$



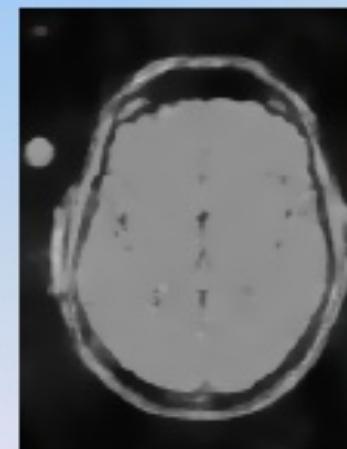
$t=12$



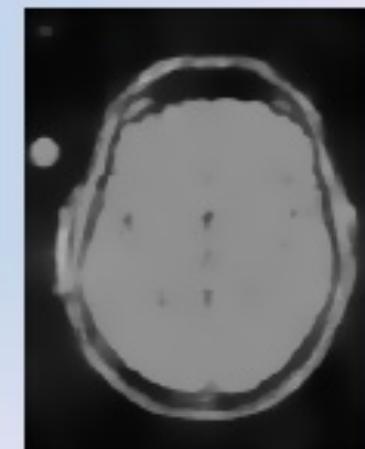
$t=16$



$t=20$



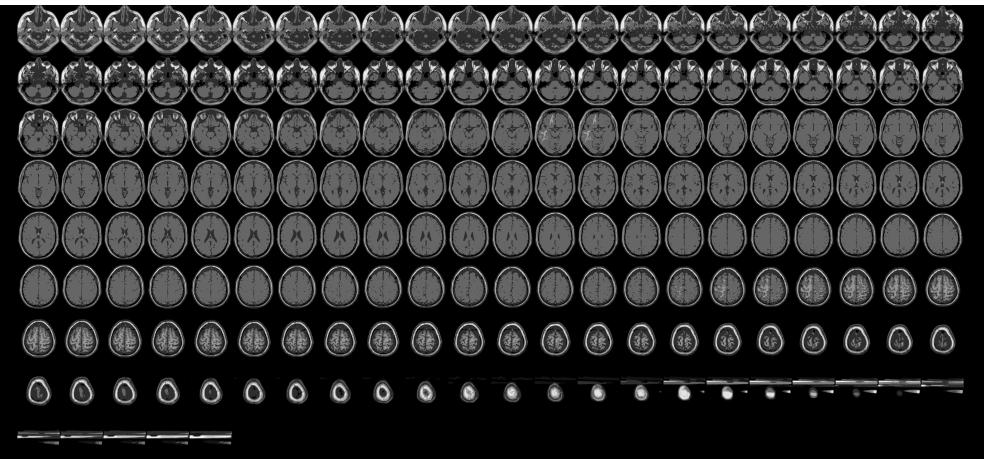
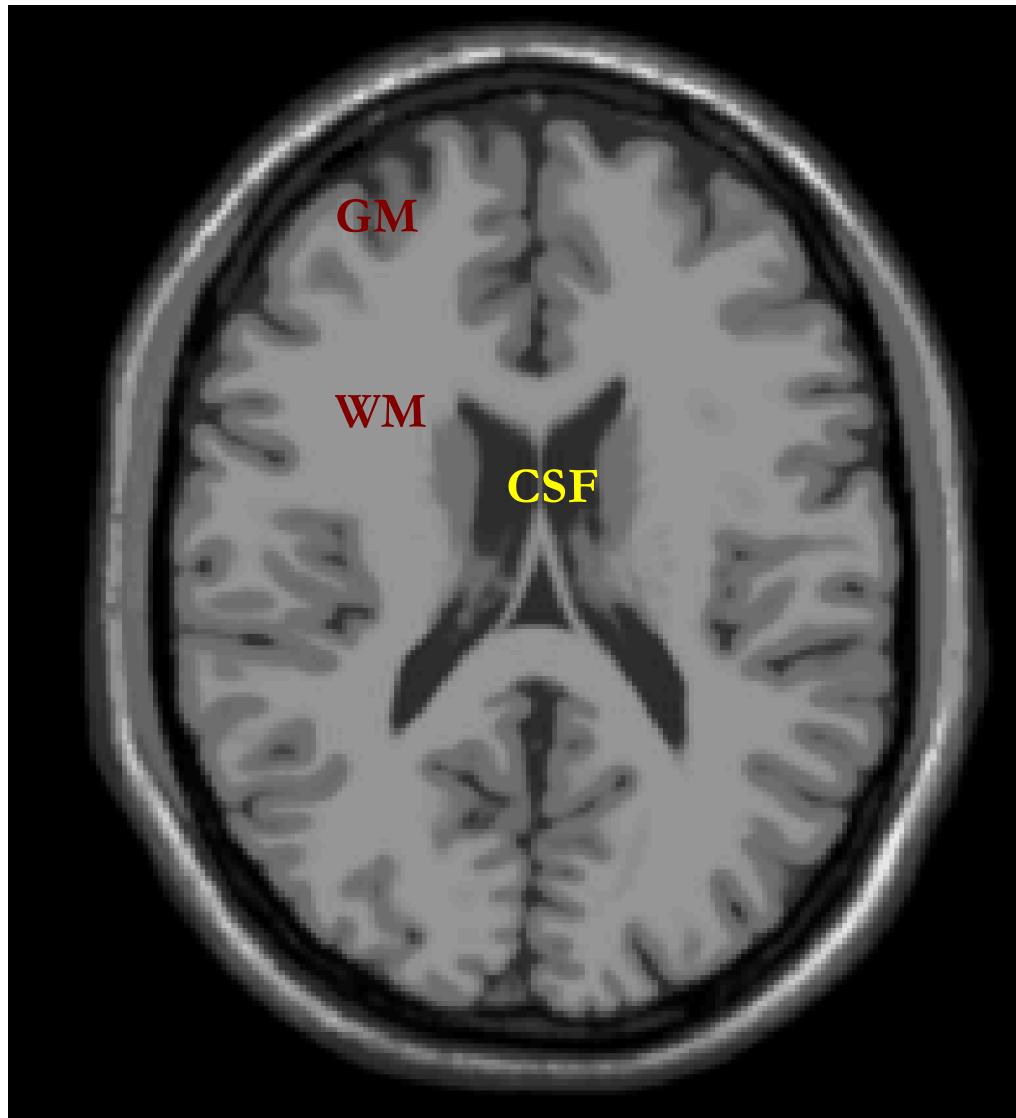
$t=24$



$t=40$



# Background: *BrainWeb*



## MR Brain simulator

**Modality:** (you can choose one of the following pulse sequences)

T1  T2  PD

**Slice thickness:** (in-plane pixel size is always 1x1mm)

1mm  3mm  5mm  7mm  9mm

**Noise:** (calculated relative to the brightest tissue)

0%  1%  3%  5%  7%  9%

**Intensity non-uniformity ("RF"):**

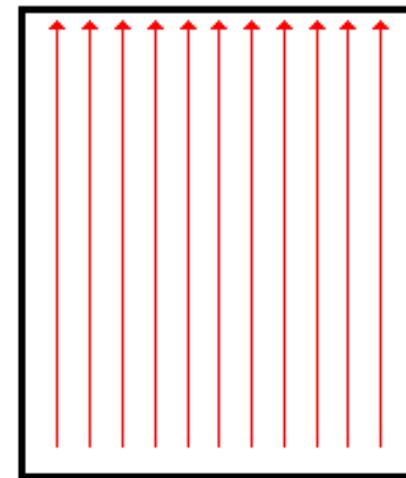
0%  20%  40%

[Reset form] [View] [Download]

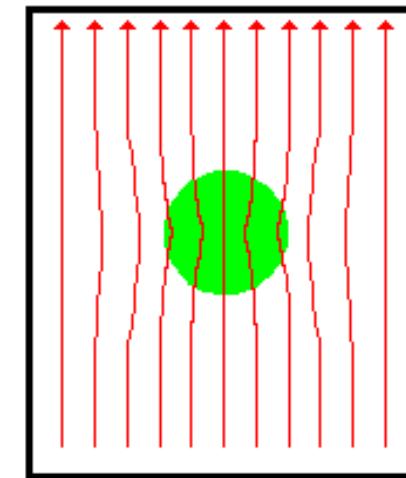
# Magnetic Field Inhomogeneity

Material	$\chi$ (ppm)
Free space	0
Air	0.4
Water	-9.14
Fat	7.79
Bone	-8.44
Grey Matter	-8.97
White Matter	-8.80

Field *inhomogeneity* is measured in parts per million (ppm) with respect to the *external field*



Normal Fields



Distorted Fields

Different tissues have different magnetic susceptibilities

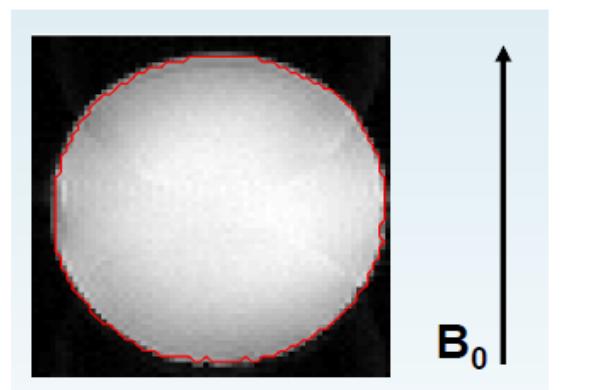
⇒ distortions in magnetic field

distortions are most noticeable near air-tissue interfaces

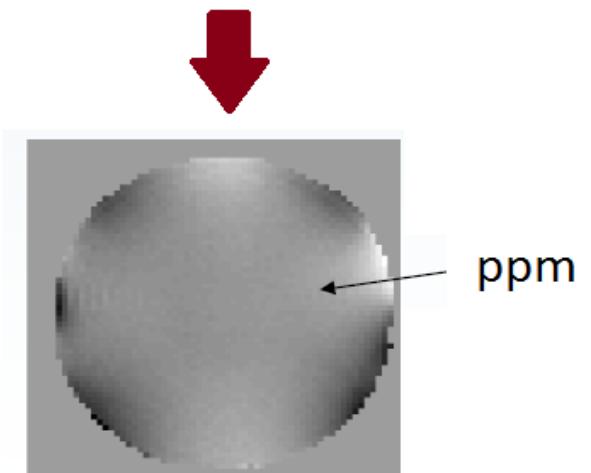
# MR Intensity Inhomogeneity

- Often hardly noticeable, but **registration, segmentation, and thus quantification** processes are significantly affected from inhomogeneity field

**Water-filled phantom in magnetic field:**



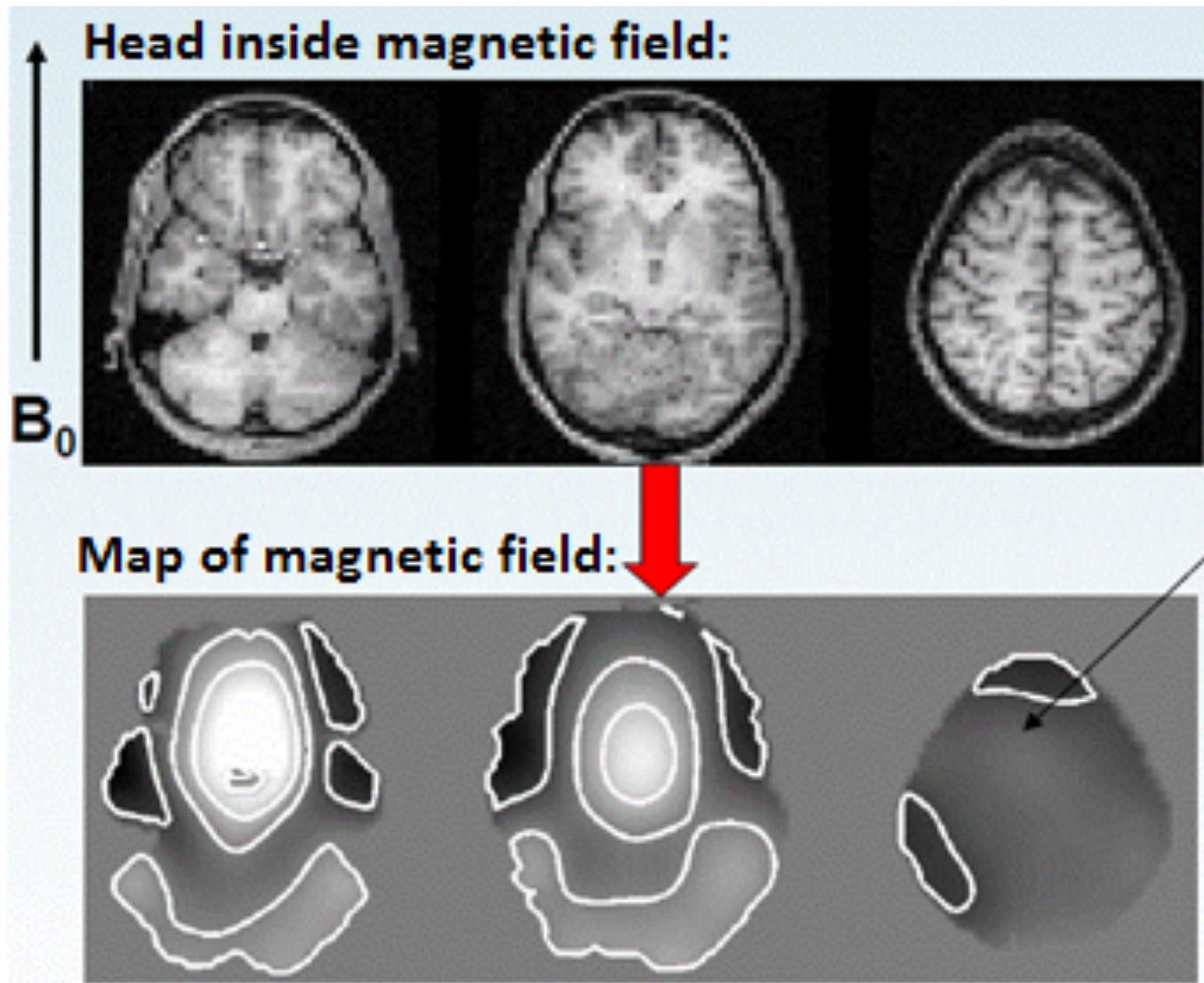
**Map of magnetic field:**



(credit: R.Gupta)



# MR Intensity Inhomogeneity



Large susceptibility variation in the human brain leads to greater field inhomogeneity and therefore image distortion.

(credit: R.Gupta)

# Intensity Inhomogeneity Correction

- **Problem:**
  - Imperfections in the ***RF field*** cause background variations in ***MR*** images.
  - Poses challenges in image segmentation and analysis.
- **Goal:** To develop a general method for correcting the variations that fulfills:
  - (R1) no need for user help per scene
  - (R2) no need for accurate prior segmentation
  - (R3) no need for prior knowledge of tissue intensity distribution

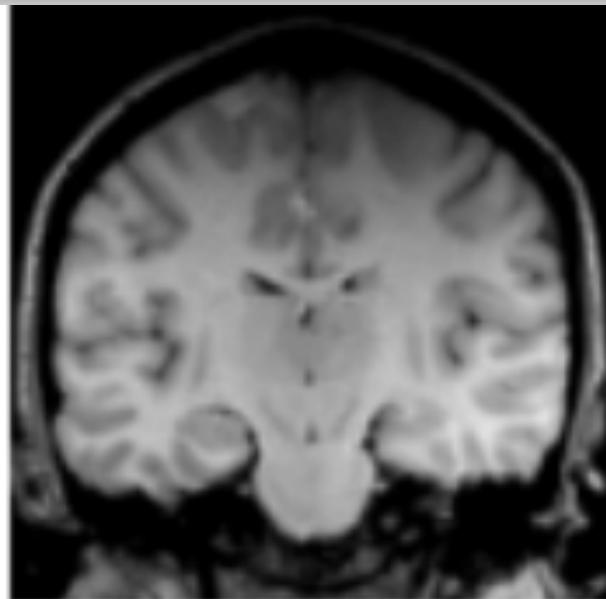
# Intensity Inhomogeneity Correction Methods

IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 26, NO. 3, MARCH 2007

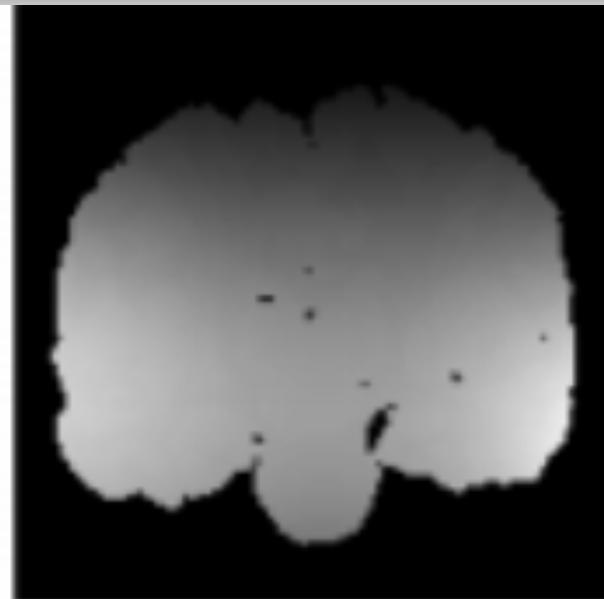
405

## A Review of Methods for Correction of Intensity Inhomogeneity in MRI

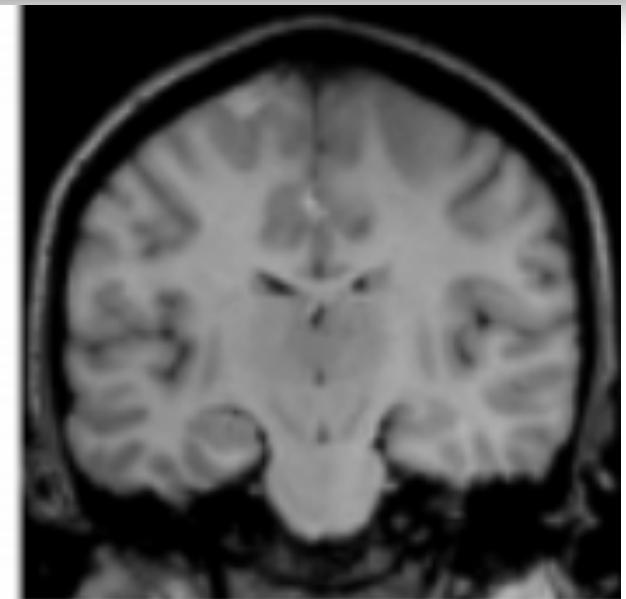
Uroš Vovk, Franjo Pernuš, and Boštjan Likar\*



Original Image



Inhomogeneity Field



Corrected Image

# Bias Correction Approaches

Numerous methods have been published in the last two decades

## I. Prospective Approaches

- i. Phantom
- ii. Multicoil
- iii. Special sequence

## II. Retrospective Approaches

- i. Filtering
- ii. Surface Fitting (intensity or gradient)
- iii. Segmentation (ML, MAP, FCM, nonparametric,...)
- iv. Histogram
  - a. High frequency maximization
  - b. Information amximization
  - c. Histogram matching

# Prospective Approaches-Phantom

- Treat intensity corruption as a systematic error of the MRI acquisition process that can either be minimized by acquiring additional images of **a uniform phantom**, by acquiring additional images with different coils, or by devising special imaging sequences.

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- Oil or water is usually used for phantoms and median filtering is applied for image smoothing.
- **Warning:** The phantom based approach cannot correct for patient-induced inhomogeneity, which is a major drawback of this approach. The remaining intensity inhomogeneity can be as high as 30%

# Prospective Approaches-MultiCoil and Special Sequences

- Volume and Surface coils
  - **Volume coil:** induce less inhomogeneity, poor SNR
  - **Surface coil:** induce severe inhomogeneity, good SNR
  - **Method:** dividing the filtered surface coil image with the body coil image and smoothing the resulting image
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- Sequence design (pulse design)
  - **Method:** the spatial distribution of the flip angle can be estimated and used to calculate the intensity inhomogeneity.
  - **Disadvantage:** Hardware design

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$$\log u(x) = \log v(x) - LPF(\log v(x)) + C_N$$

- $\log v(x)$  is input image,  $C_N$  is normalization constant,  $u(x)$  corrected image.
- However, this is true only when imaged anatomical structures are relatively small !!!

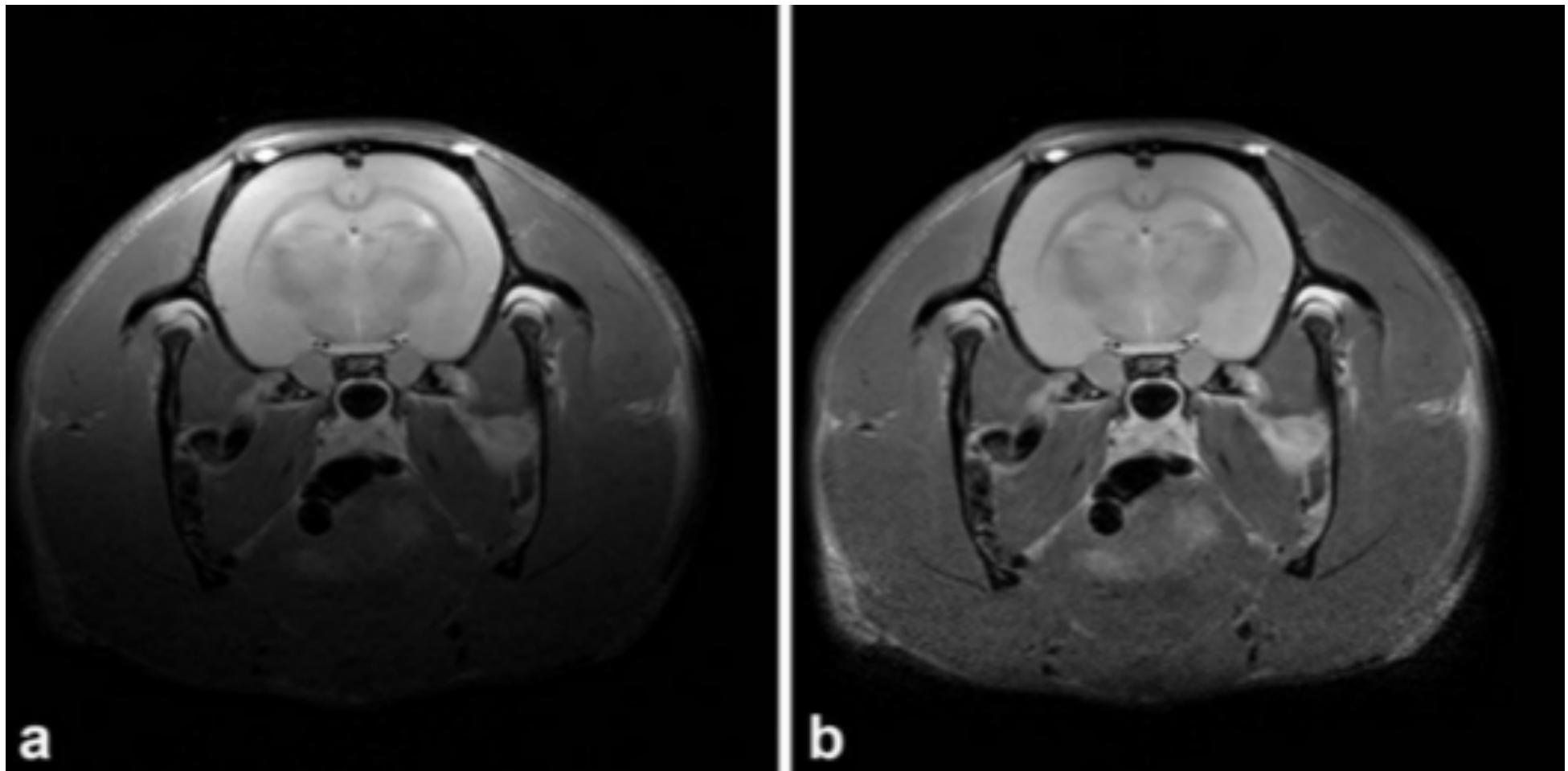
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- **FILTERING:**
  - Homomorphic unsharp masking
  - probably the simplest and one of the most commonly used methods
  - $b(x)$  (bias field) is obtained by low-pass filtering of the input image  $v(x)$ , divided by the constant  $C_N$  to preserve mean or median intensity

$$u(x) = v(x)/b(x) = v(x)C_N/LPF(v(x))$$



## Prospective Approaches-Filtering/Surface Fitting



A representative example of a slice from a rat brain. a: Original image. b: after inhomogeneity correction with the phantom based correction algorithm. Credit: Hui et al, JMRI 2010.

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- **Segmentation-based approaches:**
  - ML (maximum likelihood) or MAP (maximum a posteriori probability) criterion may be used to estimate intensity distribution in MRI
  - FCM (fuzzy c-means) for clustering tissue classes
  - Connectivity criteria is used to enforce smooth labeling

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- **Histogram-based approaches:**
  - directly on image intensity histograms
  - the inhomogeneity field is slowly varying -> it is natural to assume smooth histogram then!
  - N3 method is widely used, the method is iterative and seeks the smooth multiplicative field that maximizes the high frequency content of the distribution of tissue intensity.

IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 17, NO. 1, FEBRUARY 1998

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## A Nonparametric Method for Automatic Correction of Intensity Nonuniformity in MRI Data

John G. Sled,\* Alex P. Zijdenbos, *Member, IEEE*, and Alan C. Evans

## Nonparametric Non-uniform Intensity Normalization (N3-Sled, TMI 1998)

- Consider the following model of image formation in MR:

$$v(x) = u(x)f(x) + n(x)$$

where at location  $x$ ,  $v$  is measured signal,  $u$  is true signal,  $n$  is noise.  $f$  (bias field) is unknown.

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$$V(\hat{v}) = U(\hat{v}) * F(\hat{v})$$

# Nonparametric Non-uniform Intensity Normalization (N3-Sled, TMI 1998)

- Consider the following model of image formation in MR:

if  $u$  and  $f$  are uncorrelated random variables,  
 the distribution of their sum is found by  
 convolution!

$$\hat{v}(x) = \hat{u}(x) + f(x)$$

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$$\begin{aligned}
 E[\hat{u}|\hat{v}] &= \frac{1}{V(\hat{v})} \int_{-\infty}^{\infty} \hat{u} p(\hat{u}, \hat{v}) d\hat{u} \\
 &= \frac{1}{V(\hat{v})} \int_{-\infty}^{\infty} \hat{u} p(\hat{u}, \hat{f}) d\hat{u} \\
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 \hat{f}_e(\hat{v}) &= E[\hat{f}|\hat{v}] = \hat{v} - E[\hat{u}|\hat{v}]
 \end{aligned}$$

The method is based on to maximize the frequency content of the image intensity distribution.

# Nonparametric Non-uniform Intensity Normalization (N3-Sled, TMI 1998)

1. Use log domain, and prob. densities of  $u, v$ , and  $f$ .
2. Guess a kernel  $f$ , and estimate  $u$ ! (since  $V(\hat{v}) = U(\hat{v}) * F(\hat{v})$  )
3. Iterate this process until convergence

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## Nonparametric Non-uniform Intensity Normalization (N3-Sled, TMI 1998)

1. Use log domain, and prob. densities of  $u, v$ , and  $f$ .

The approach is simply to propose a distribution for  $\mathbf{U}$  by **sharpening** the distribution  $\mathbf{V}$ , and then to estimate a corresponding smooth field  $\mathbf{F}$  which produces a distribution close to the one proposed.

How do we guess  $f$ ? ( $\mathbf{F}$ ?)

- $\mathbf{F}$  is set to be Gaussian field with small variance!

# ITK Implementation of N3

- **itkN3MRIBiasFieldCorrectionImageFilterTest**

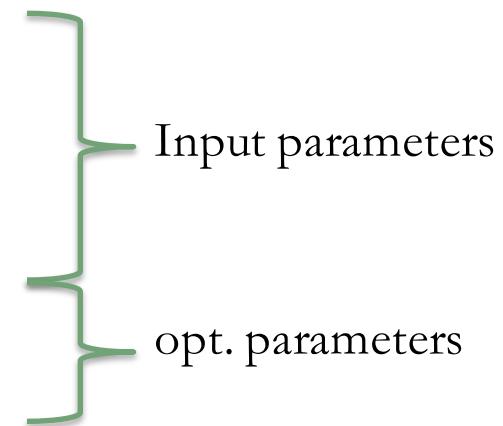
imageDimension

inputImage

outputImage

[shrinkFactor] [maskImage] [numberOfIterations]

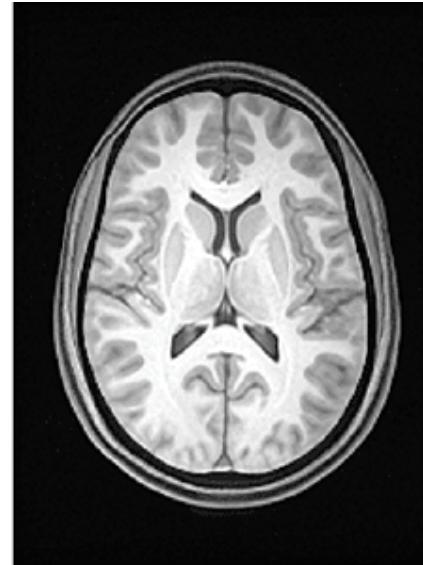
[numberOfFittingLevels] [outputBiasField]



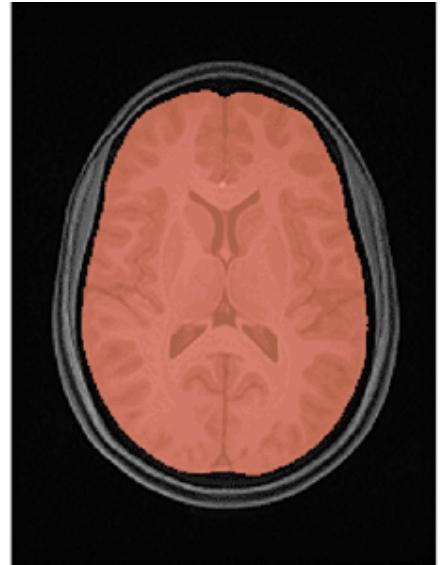


# ITK Implementation of N3

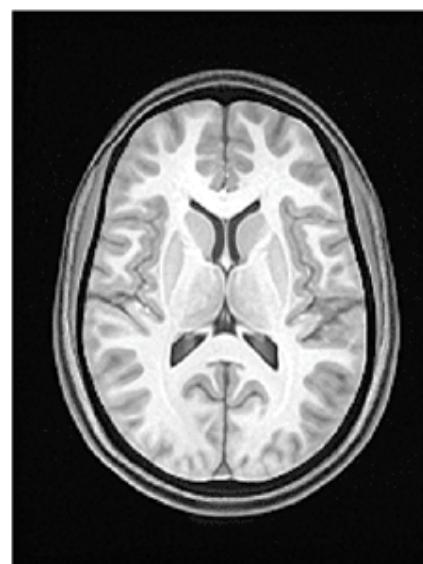
- `itkN3MRIBiasFieldCorrectionImageFilter`  
`imageDimension`  
`inputImage`  
`outputImage`  
`[shrinkFactor] [maskImage] [numb`  
`[numberOfFittingLevels] [outputBi`



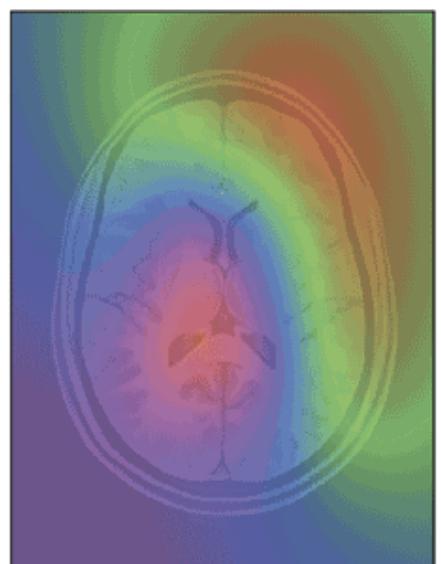
(a)



(b)



(c)



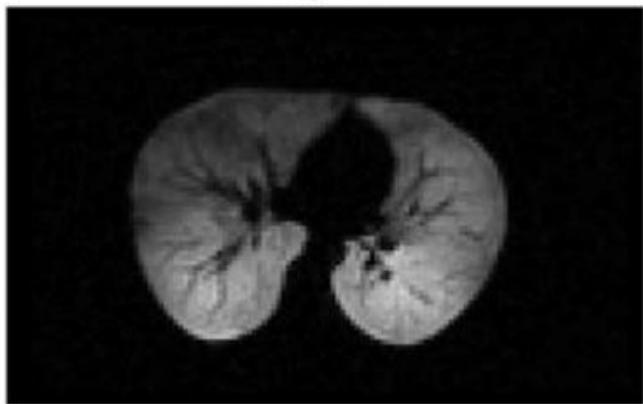
(d)

`itkN3MRIBiasFieldCorrectionImageFilterTest`  
2 `t81slice.nii.gz` `t81corrected.nii.gz`  
2 `t81mask.nii.gz` 50 4 `t81biasfield.nii.gz`



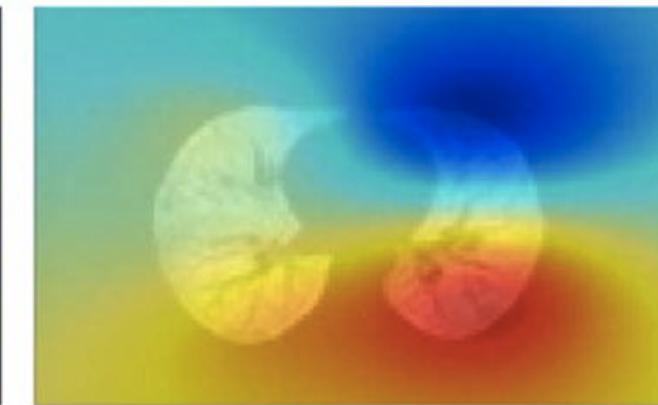
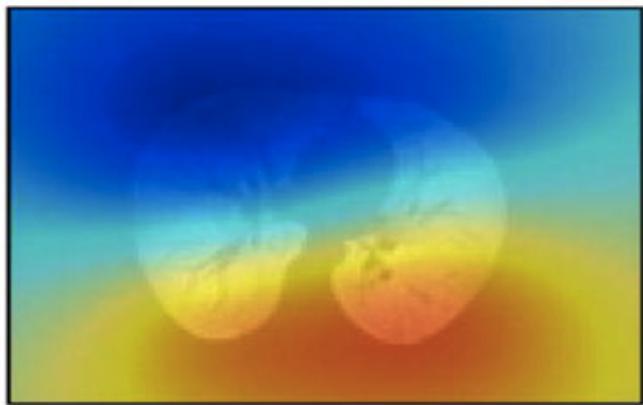
Subject 1

Uncorrected

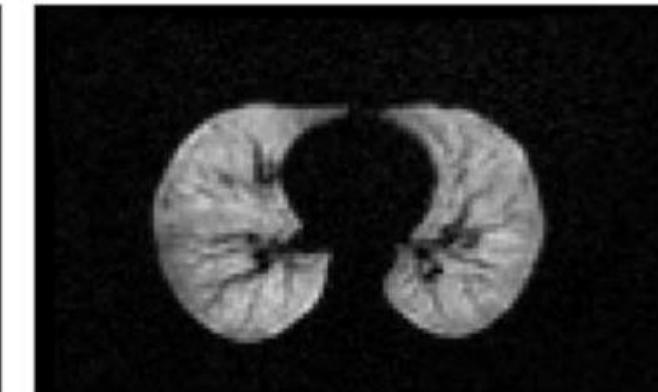


Subject 2

Bias Field



Corrected  
(N3 based  
method)



# Local Histogram Based and Standardization Based Correction Methods

- Dividing the image into small subvolumes (via fixed thresholding for instance) in which intensity inhomogeneity was supposed to be relatively constant.

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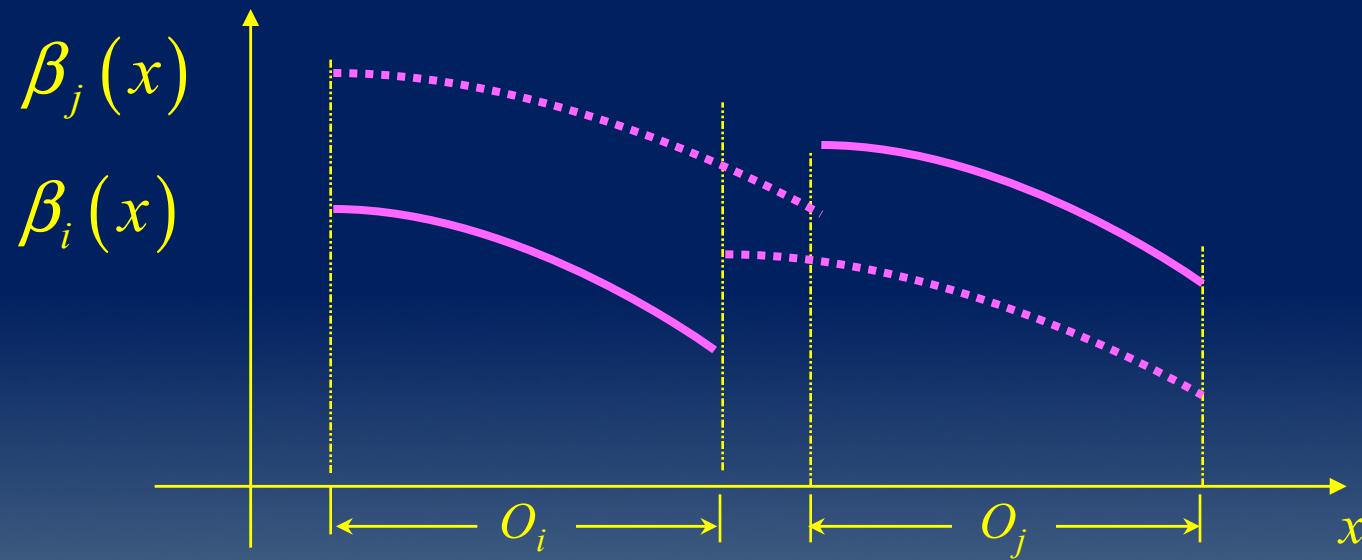
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- Local intensity inhomogeneity was estimated by least square fitting of the intensity histogram model to the actual histogram of a subvolume
- The applied histogram model was a finite Gaussian mixture with seven parameters, initialized from the global histogram of the image. (B-splines are used to fit parameters)

## Better (Simpler) Method – Standardization Based Correction (SBC)

- Step 0:** Set  $S_c = S$ , the given scene.
- Step 1:** Standardize  $S_c$  to the standard intensity gray scale for the particular imaging protocol and body region under consideration and output scene  $S_s$ ;
- Step 2:** determine  $m$  tissue regions  $S_{B1}, S_{B2}, \dots, S_{Bm}$  by using fixed threshold intervals on  $S_s$ ;
- Step 3:** if  $S_{Bi}$  determined in the previous iteration are not much ( $<0.1\%$ ) different from the current  $S_{Bi}$ , stop;
- Step 4:** else, estimate background variation in  $S_s$  as a scene  $S_{be}$ , compute corrected scene  $S_c$ , and go to Step 1;



## SBC-Intuition



The existence of discontinuity between inhomogeneity maps (continuous lines) estimated independently from different tissue regions  $O_i$  and  $O_j$ .

We need a single combined inhomogeneity map for correcting the background intensity variation in the whole image.

## SBC-Intuition

1. Find a weight factor  $\lambda$  to minimize  $\sum_{c \in C} [\beta_1(c) - \lambda \beta_2(c)]^2$ .
2. Combine the two inhomogeneity maps  $\beta_1$  and  $\beta_2$  to obtain a new discrete inhomogeneity map  $\beta_d(c)$ :  $C \rightarrow [0, \infty)$  such that, for any  $c \in C$ ,

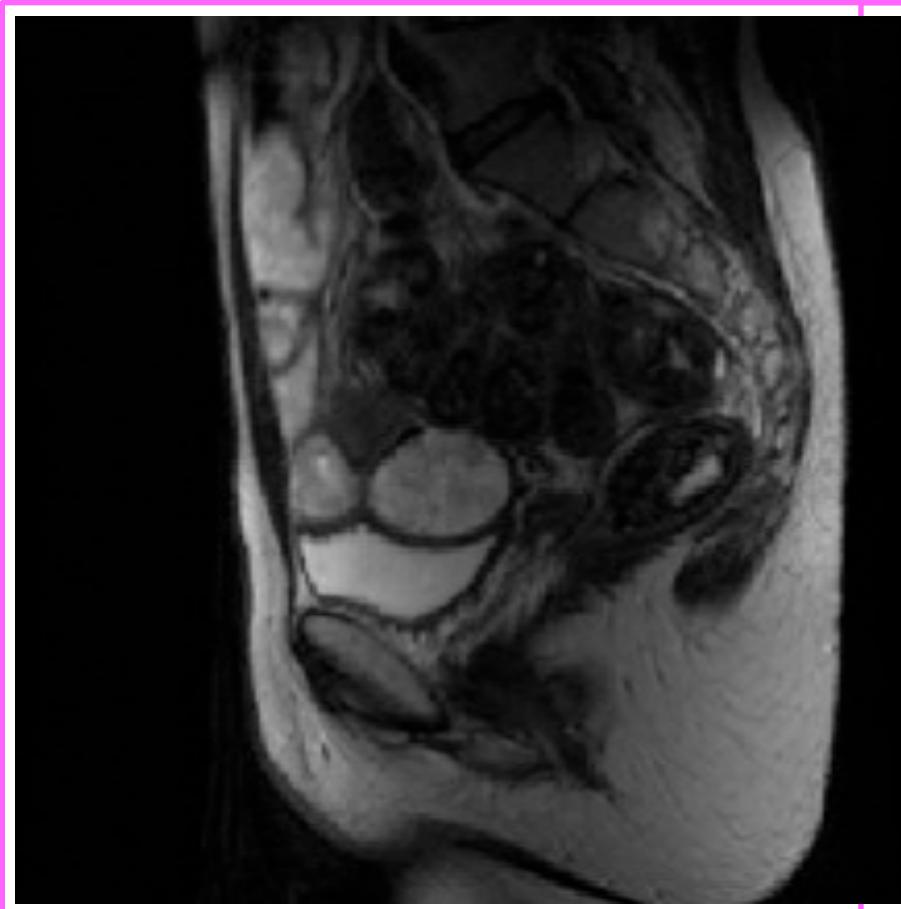
$$\beta_d(c) = \frac{\delta(c, O_2)}{\delta(c, O_1) + \delta(c, O_2)} \beta_1(c) + \frac{\delta(c, O_1)}{\delta(c, O_1) + \delta(c, O_2)} \lambda \beta_2(c)$$

3. Determine a 2<sup>nd</sup> degree polynomial  $\beta$  that constitutes a *LSE* fit to  $\beta_d$ .

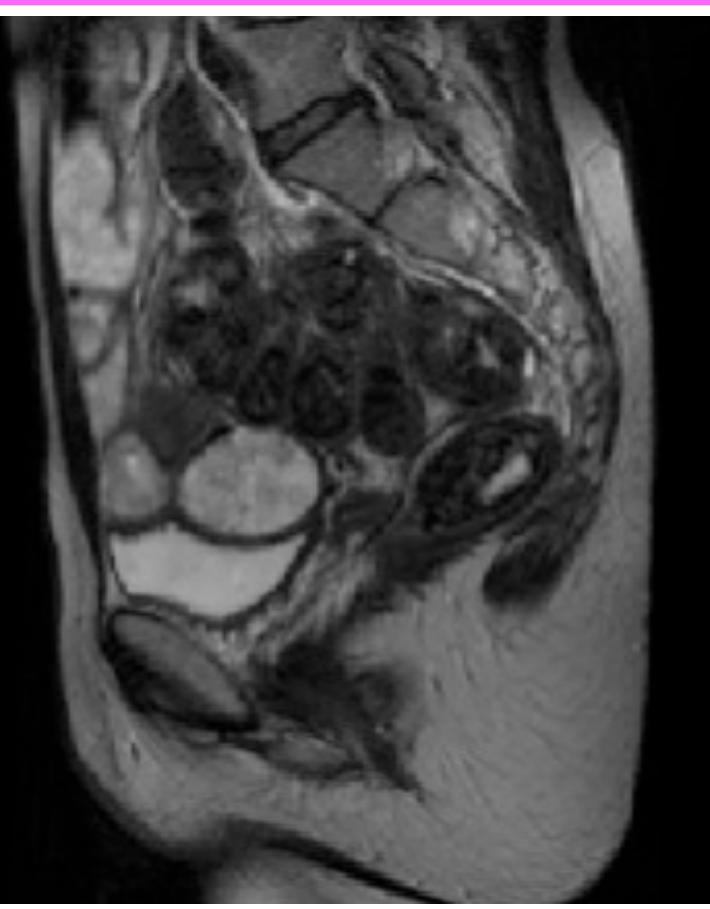
The above steps merge  $O_1$  and  $O_2$  and are then repeated until we have only one region and a single unified inhomogeneity map.



Original



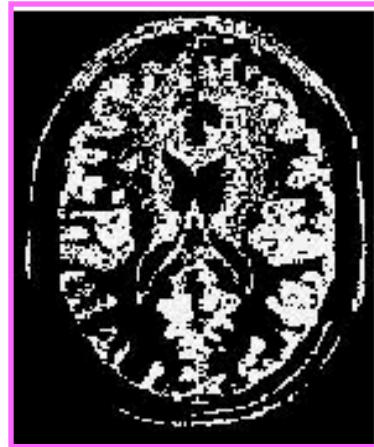
Corrected



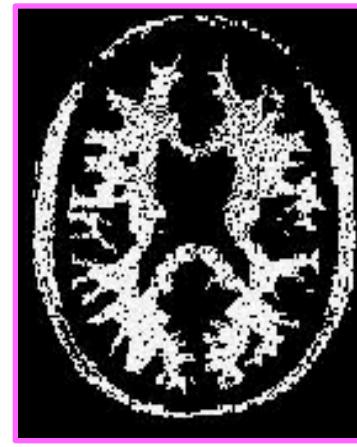


# Standardization Based Correction (SBC) Method

GM



WM



Iteration 1

3

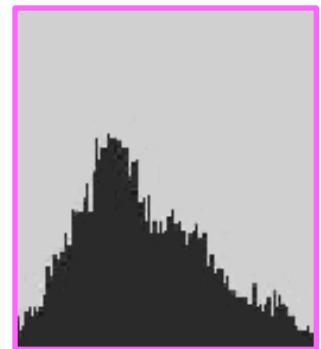
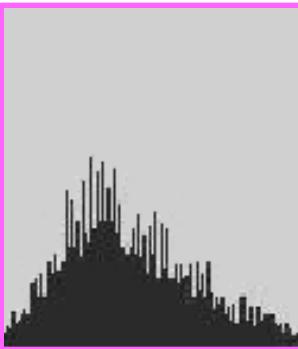
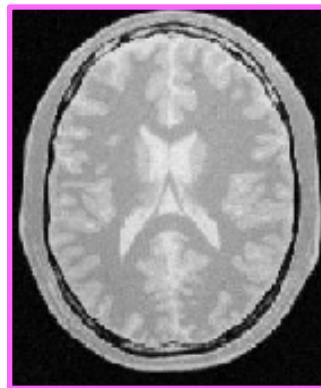
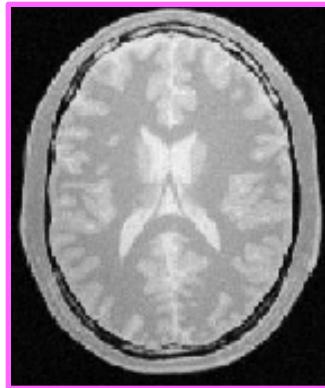
5

10

20

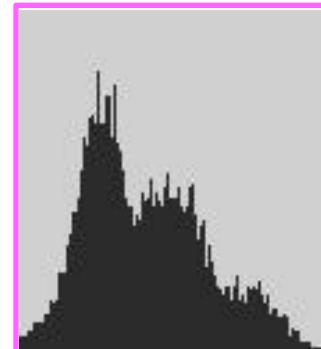
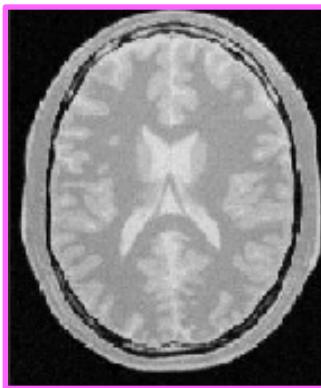


## SBC Method

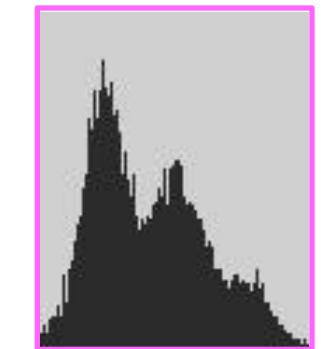
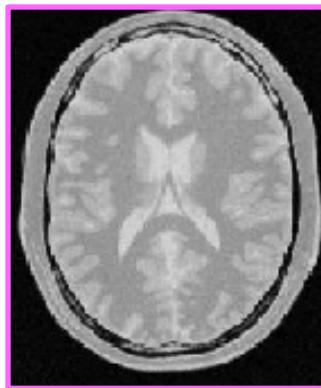


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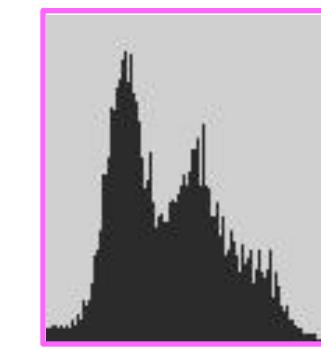
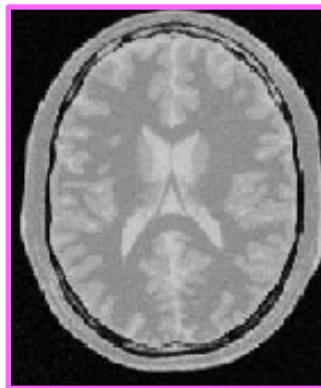
3



5



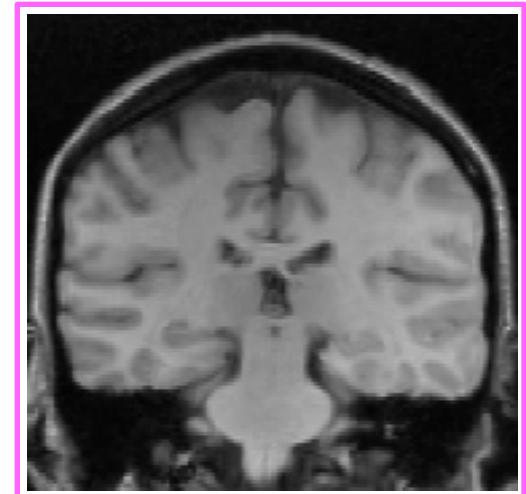
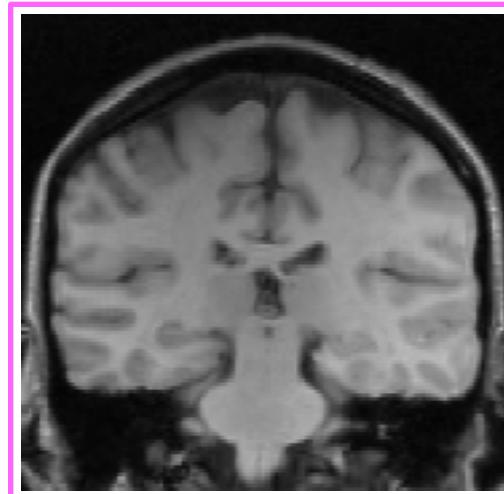
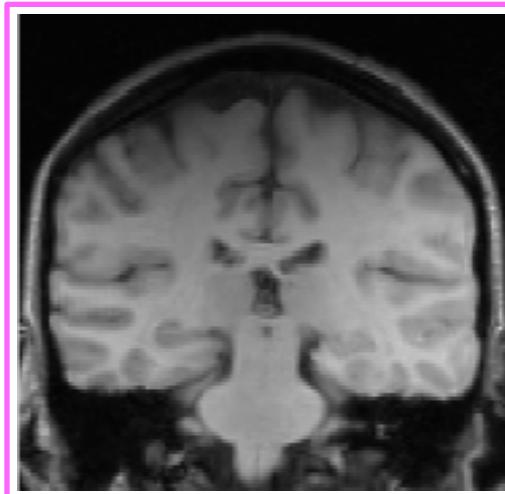
10



20

The improvement in correction with increasing number of iterations. Examine the two modes corresponding to *WM* (large mode) and *GM*.

## SBC Method-Comparison



Original



*N3 (Sled *et al.*)*

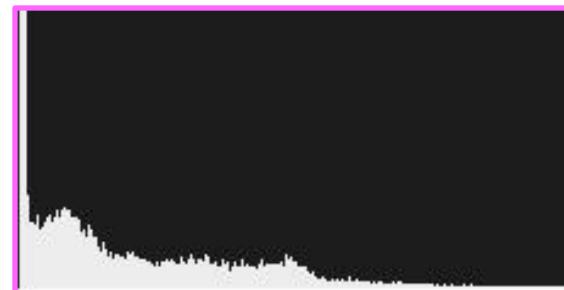
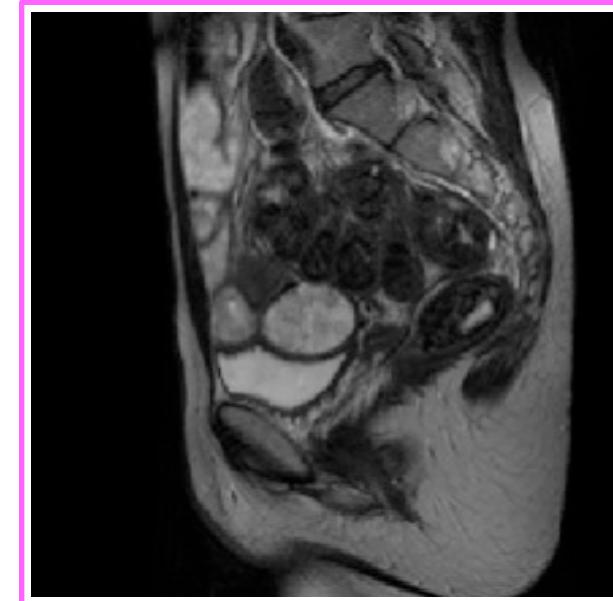
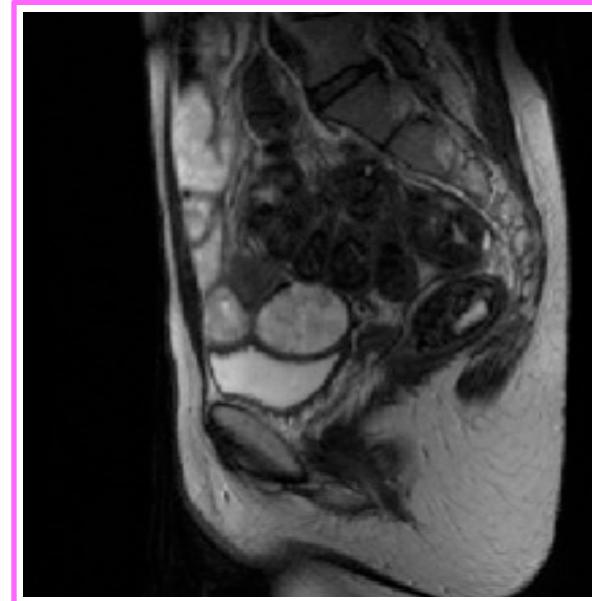
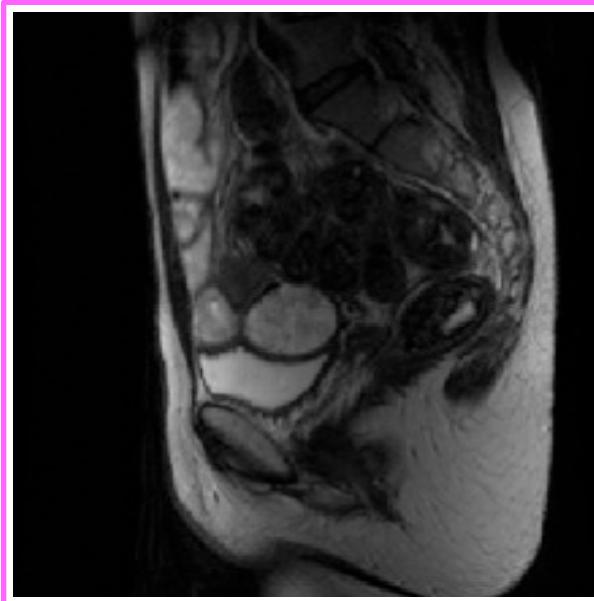


*SBC*

A slice of *T1*-weighted brain *MR* image. *SBC* shows some improvement over *N3* particularly as seen in the histogram.



## SBC Method-Comparison



Original

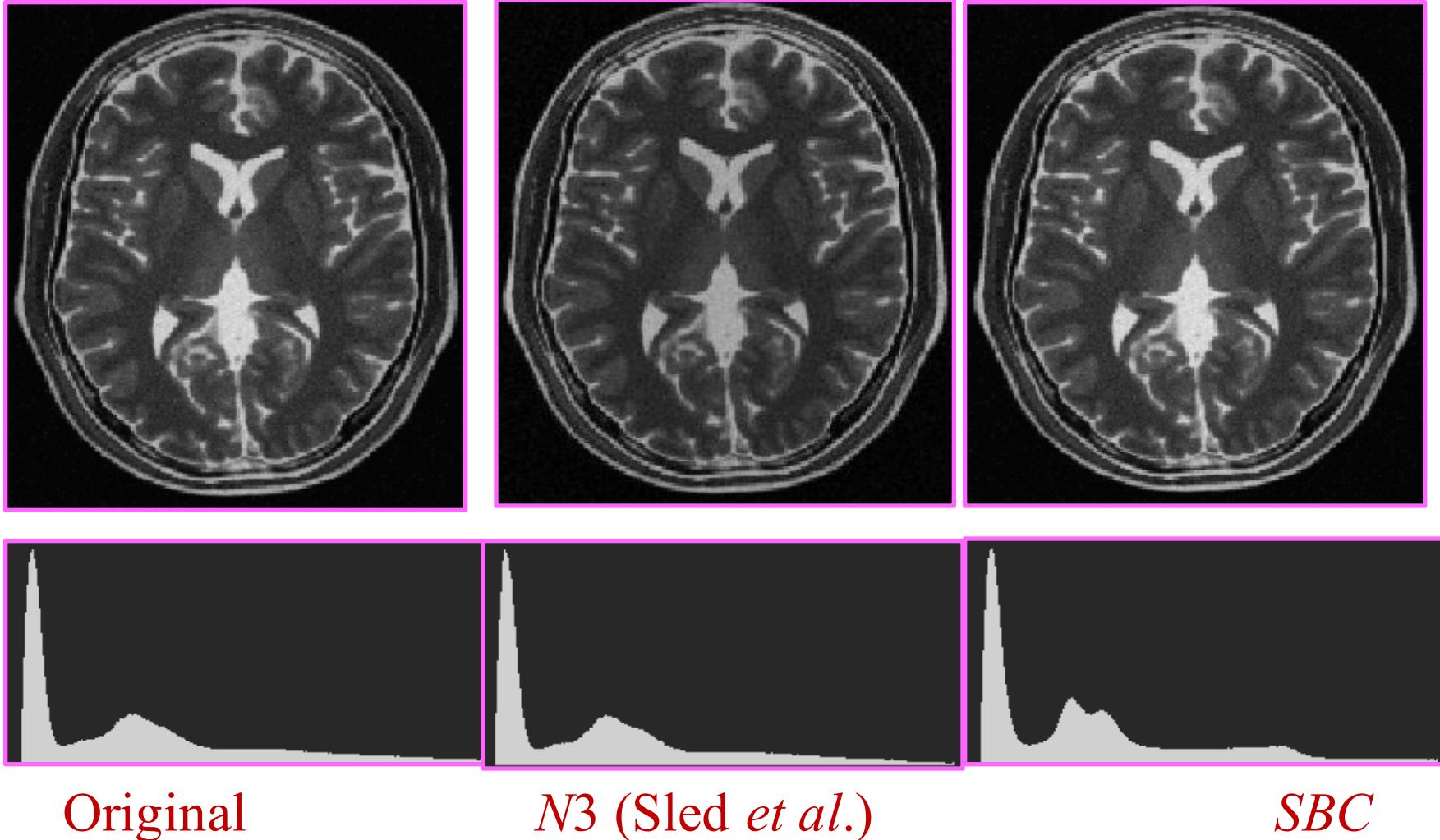
*N3 (Sled *et al.*)*

*SBC*

A slice of an abdominal *MR* image. *SBC* shows some improvement over *N3* particularly as seen in the histogram.



## SBC Method-Comparison



*Brainweb* T2-weighted MR image. *SBC* shows some improvement over *N3* particularly as seen in the histogram.

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# SBC Method Quantitative Comparison

Set	Modality	Inhomo.	%cv (GM)			%cv (WM)		
			Original	N3	SBC	Original	N3	SBC
Normal	<i>T1</i>	20%	11.0	9.9	9.9	6.7	5.1	5.1
		40%	13.5	10.0	9.9	9.2	5.2	5.2
	<i>T2</i>	20%	18.4	18.0	17.9	12.0	11.8	11.7
		40%	20.3	20.0	17.9	13.3	13.0	11.8
	<i>PD</i>	20%	6.3	4.6	4.5	5.5	4.7	4.7
		40%	9.7	4.6	4.5	7.5	4.6	4.6
Ms Lesions	<i>T1</i>	20%	11.2	10.1	10.1	6.9	5.3	5.3
		40%	13.7	10.2	10.1	9.3	5.3	5.4
	<i>T2</i>	20%	10.9	10.0	9.8	8.7	8.3	8.1
		40%	13.7	10.1	9.8	10.6	8.2	8.2
	<i>PD</i>	20%	5.8	3.9	3.8	5.3	4.4	4.3
		40%	9.4	4.9	3.9	7.4	4.3	4.3

% cv of tissue intensities in segmented *GM* and *WM* regions for twelve simulated *MRI* scenes from *Brainweb* before and after correction by *N3 SBC*.

# SBC Method Quantitative Comparison

<b>Modality</b>	% <i>cv</i> ( <i>GM</i> )			% <i>cv</i> ( <i>WM</i> )		
	<b>Original</b>	<b><i>N3</i></b>	<b><i>SBC</i></b>	<b>Original</b>	<b><i>N3</i></b>	<b><i>SBC</i></b>
<b><i>T2</i></b>	16.7(1.61)	14.9(1.18)	14.7(1.23)	12.9(1.12)	11.5(1.07)	11.2(0.98)
<b><i>PD</i></b>	7.1(0.32)	5.9(0.20)	5.6(0.19)	7.8(0.72)	6.6(0.62)	6.2(0.51)

The mean and standard deviation of % *cv* of tissue intensities in segmented *GM* and *WM* regions for ten clinical *T2*- and *PD*-weighted *MRI* scenes of *MS* patients before and after correction by the *N3* and *SBC* methods.

*SBC* > *N3*;  $p < 0.001$ .

# References and Slide Credits

- Jayaram K. Udupa, MIPG of University of Pennsylvania, PA.
- P. Suetens, Fundamentals of Medical Imaging, Cambridge Univ. Press.
- N. Bryan, Intro. to the science of medical imaging, Cambridge Univ. Press.
- N. Agam (toy examples)
- Next Lecture (Preprocessing of Medical Images III)
  - Intensity Standardization in MR Images
  - PET/SPECT Image Denoising (multiplicative noise)