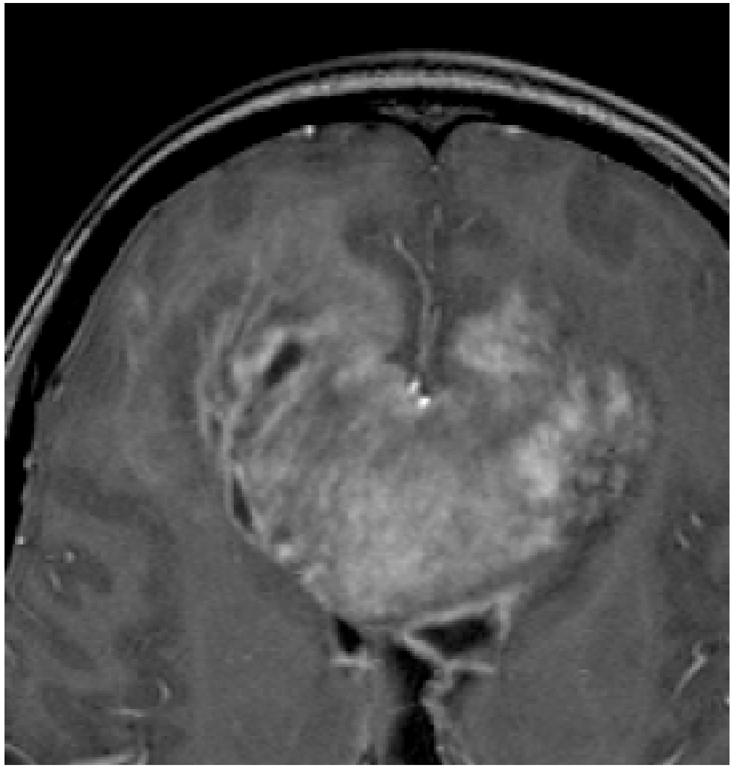
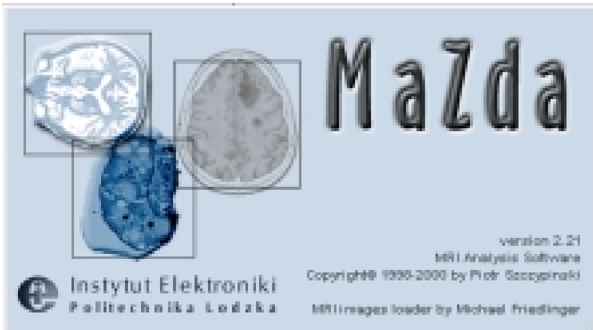
Multicenter trial - glioblastoma texture evaluation and corresponding texture feature maps

Arvid Lundervold, University of Bergen, Norway

COST B11 - WG 3, Angers 18-19 October, 2001





The data are available on the lodz server under
/home/costb11/lothar/clinical examples/763/
763-2-*.ima: fl3d 20/6/25°   prae
763-4-*.ima: fl3d 20/6/25°   post
763-3-*.ima: tse   5000/14,85   prae

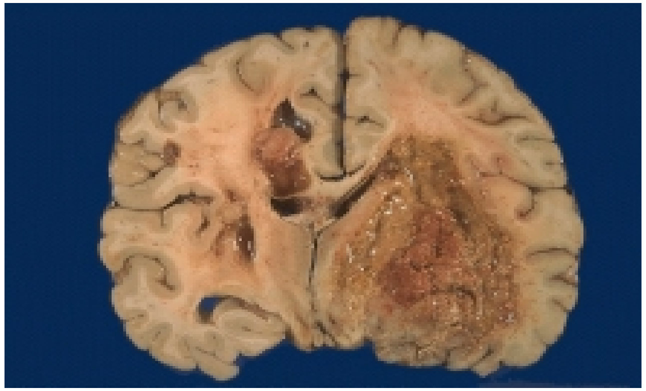
Outline

- Histology, MRI methods and textural characteristics of human and experimental glioma

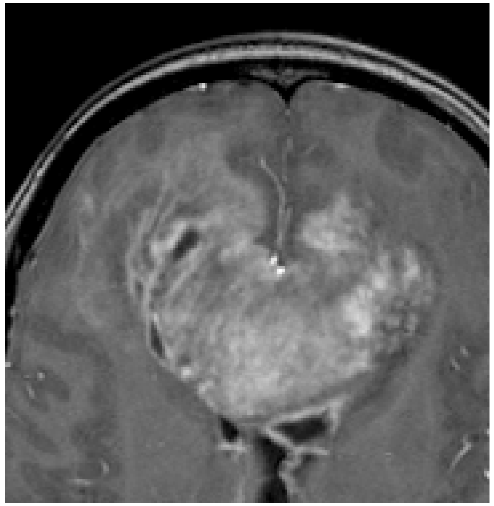
- Texture analysis and texture feature maps in multispectral images of glioblastoma acquired at DKFZ (study 763)

- Some conclusions and perspectives ...

- Glioblastoma multiforme (GBM) is the most aggressive form of the primary brain tumors known collectively as gliomas.



- These tumors arise from the supporting, glial cells of the brain during childhood and in adults.

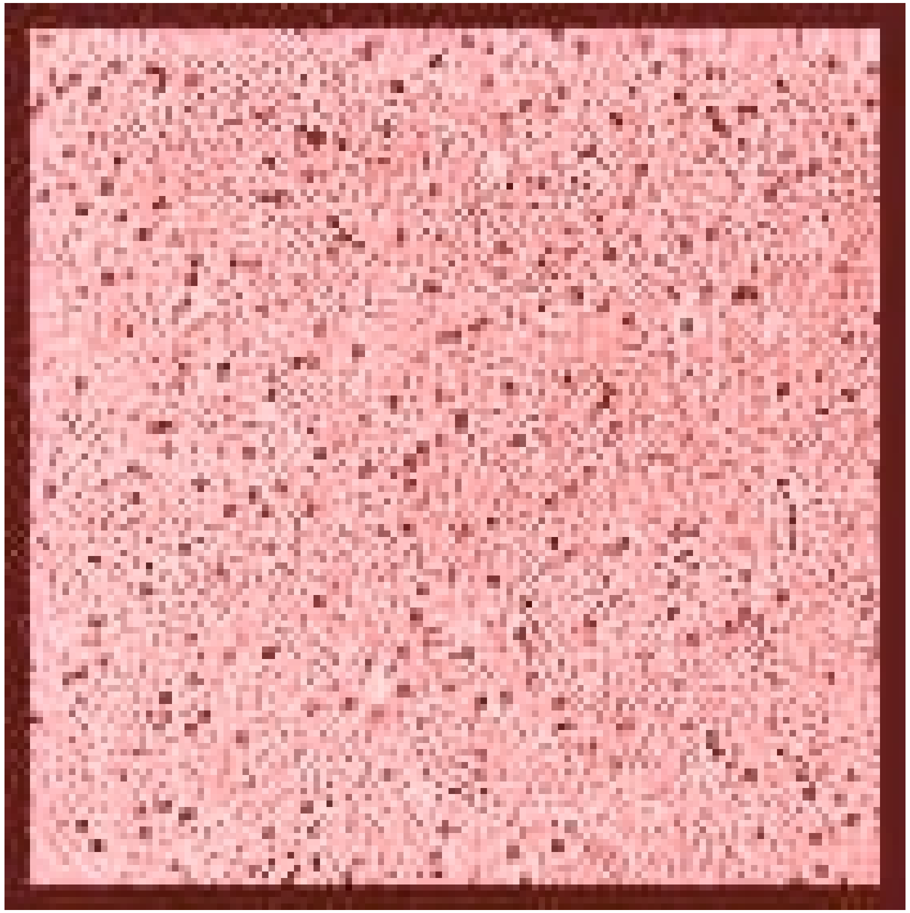


- Gliomas do not spread throughout the body like other forms of cancer, but cause symptoms by invading the brain.

- Gliomas are graded by their microscopic appearance.

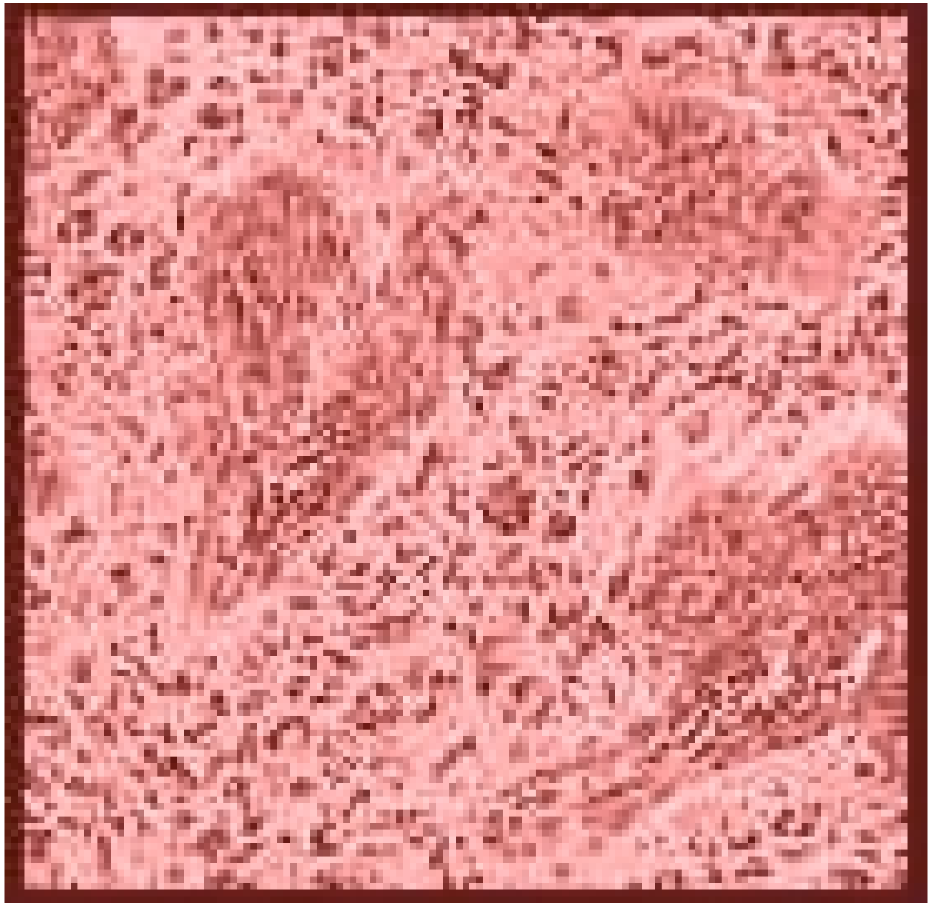
- As a rule their behavior can be predicted from this histology:
  - grade I (pilocytic astrocytomas) and
  - grade II (benign astrocytomas) tumors grow slowly over many years
  - grade IV (GBM) grows rapidly, invading and altering brain function, and untreated, GMB's are rapidly lethal.

Normal WM



Monotonous appearance of normal brain white matter under the microscope

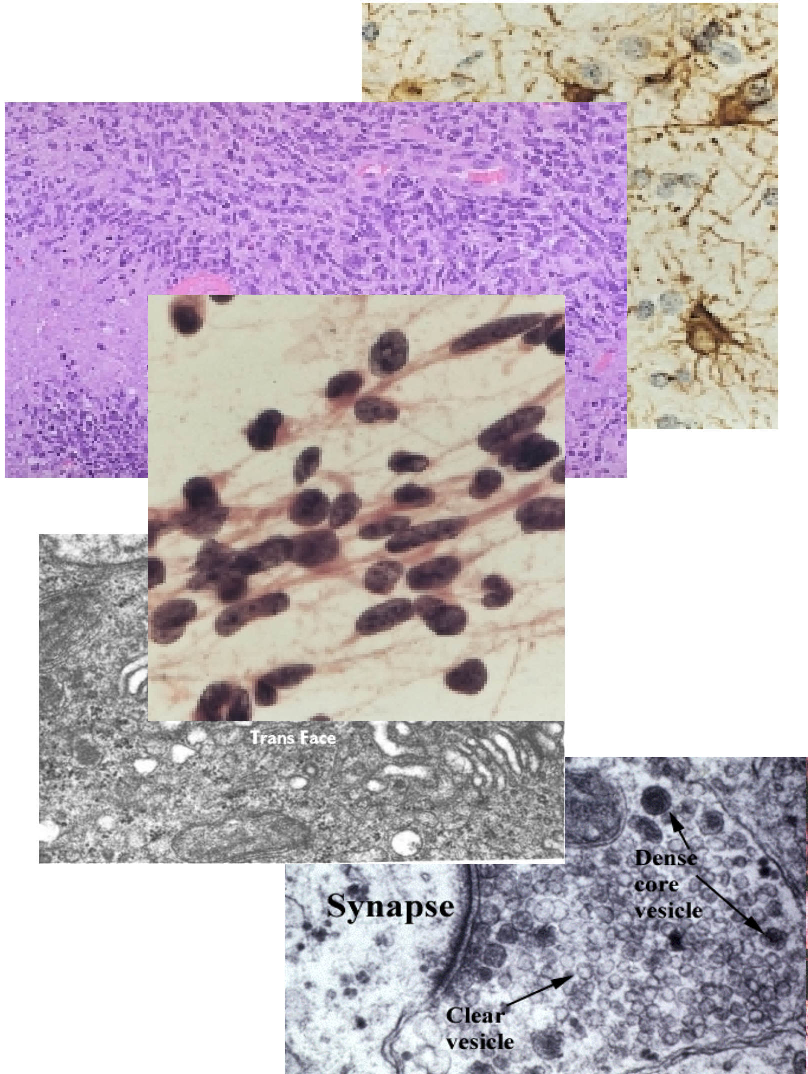
Glioblastoma



GBM contains atypical cells, dividing cells, necrosis and clumps of cells around blood vessels

http://www.sd-neurosurgeon.com/diseases/glioblastoma.html

Tumor characterization



“ Viability ”

“ Cellularity ”

“ Vascularization ”

“ Necrosis “

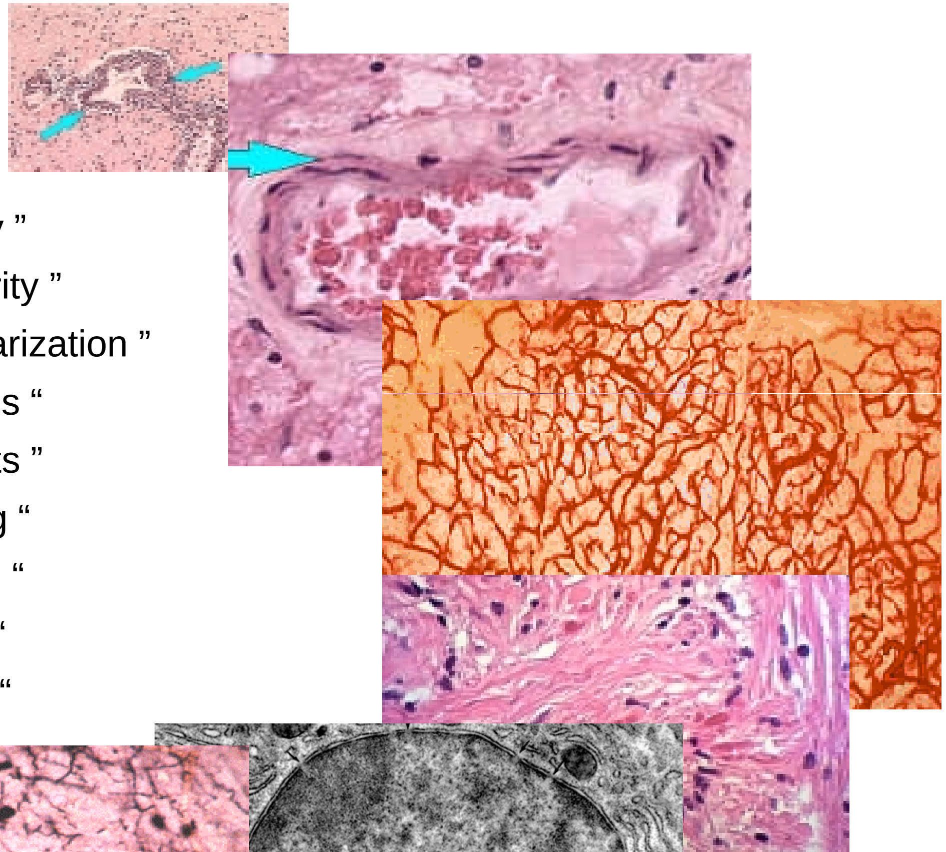
“ Deposits ”

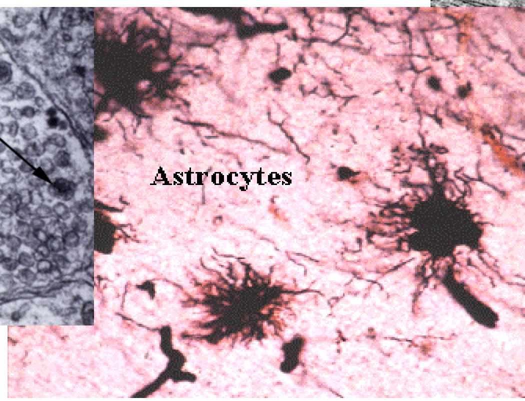
“ Grading “

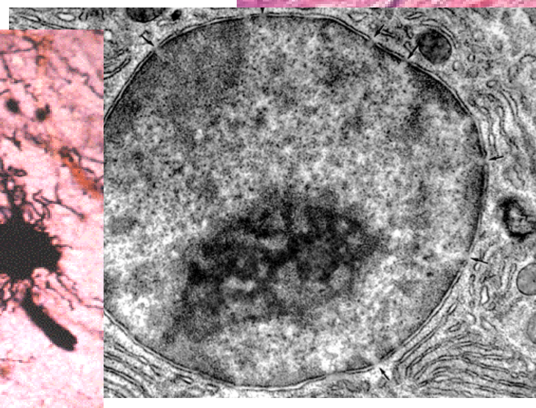
“ Staging “

“ Edema“

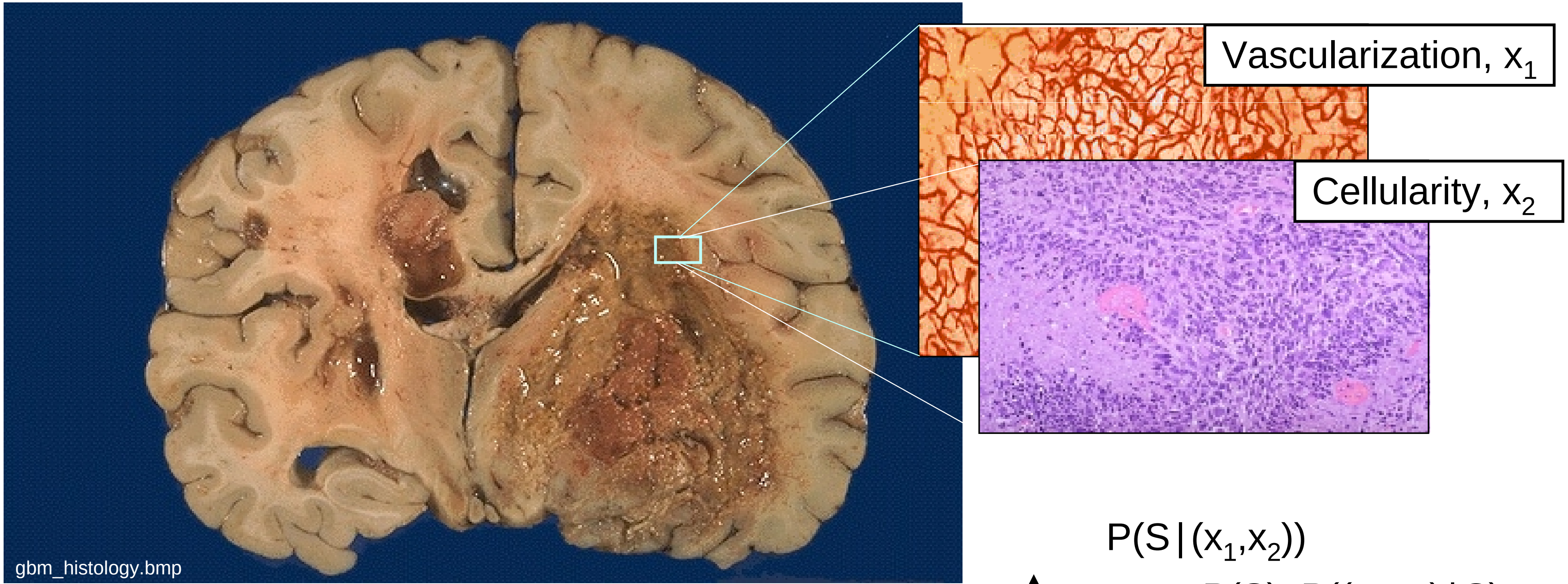
“ . . . . . “





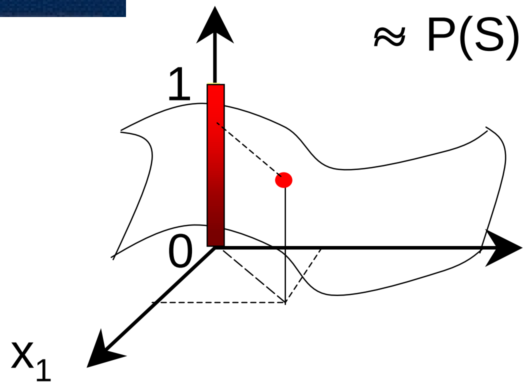


“Compute” the probability of tumor tissue state (S) given the MR measurements or features $(x_1,x_2,\ldots,x_p)$



$$P(S\,|\,(x_1,x_2)) \approx P(S)\cdot P((x_1,x_2)\,|\,S)$$

Baysian framework:



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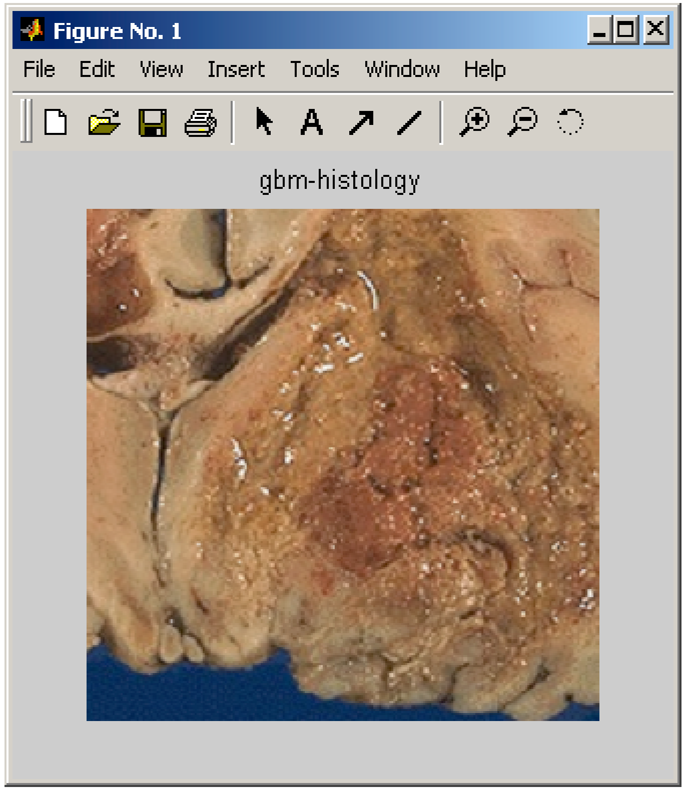
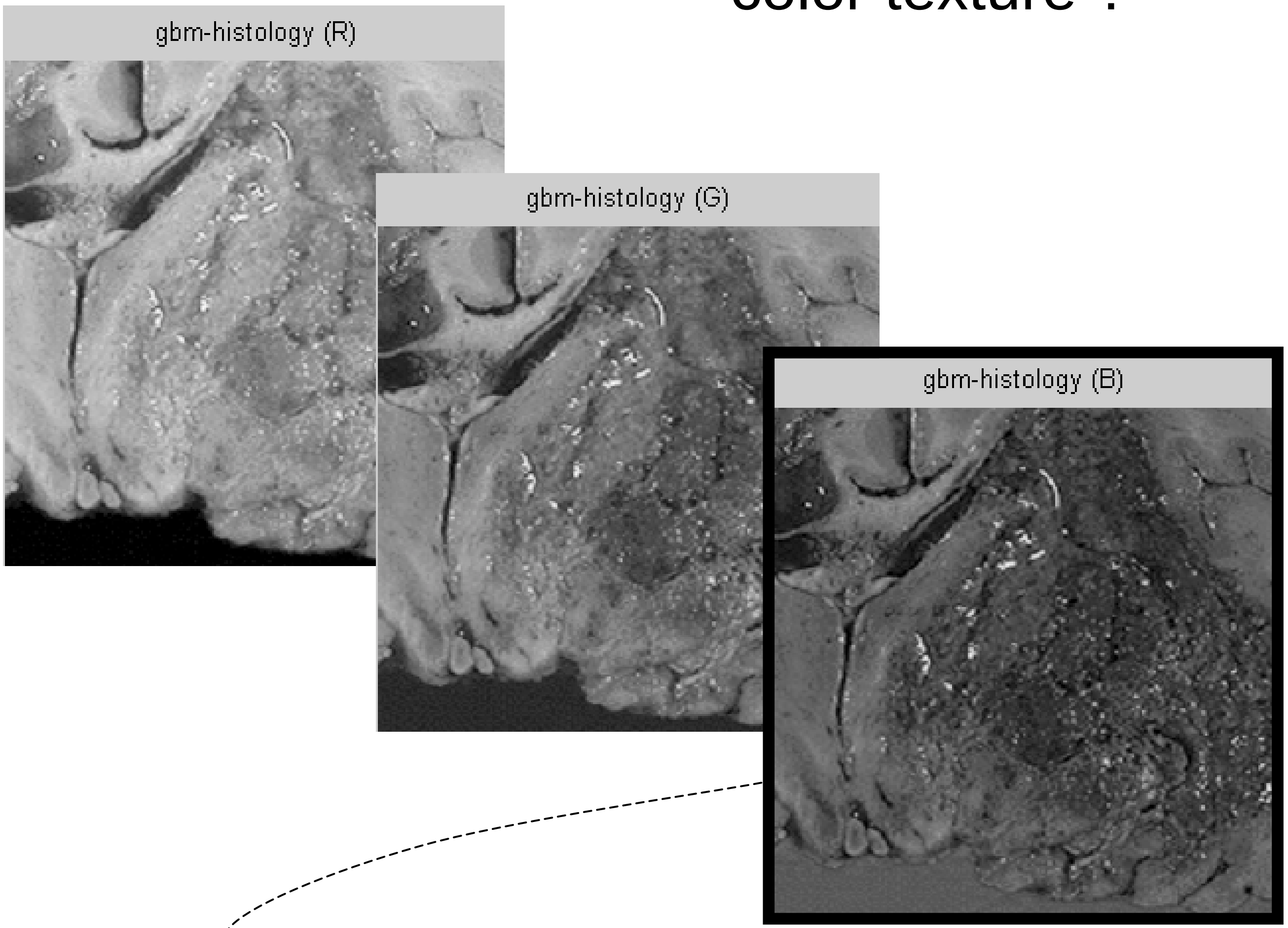


color texture ?




```
a = imread('gbm_histology.bmp');
b = a(150:150+255,300:300+255,:);
```

and texture feature maps …. →

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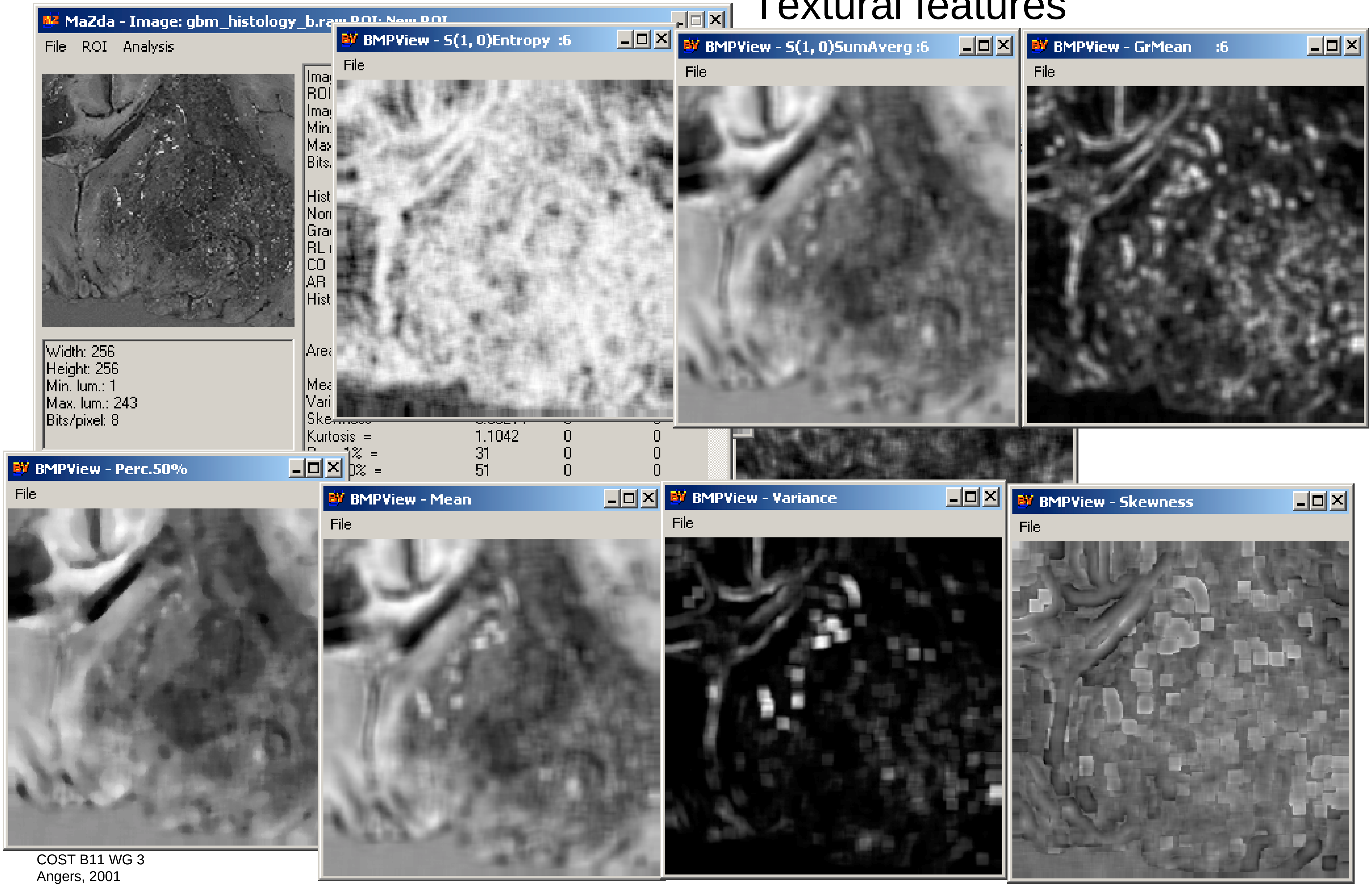
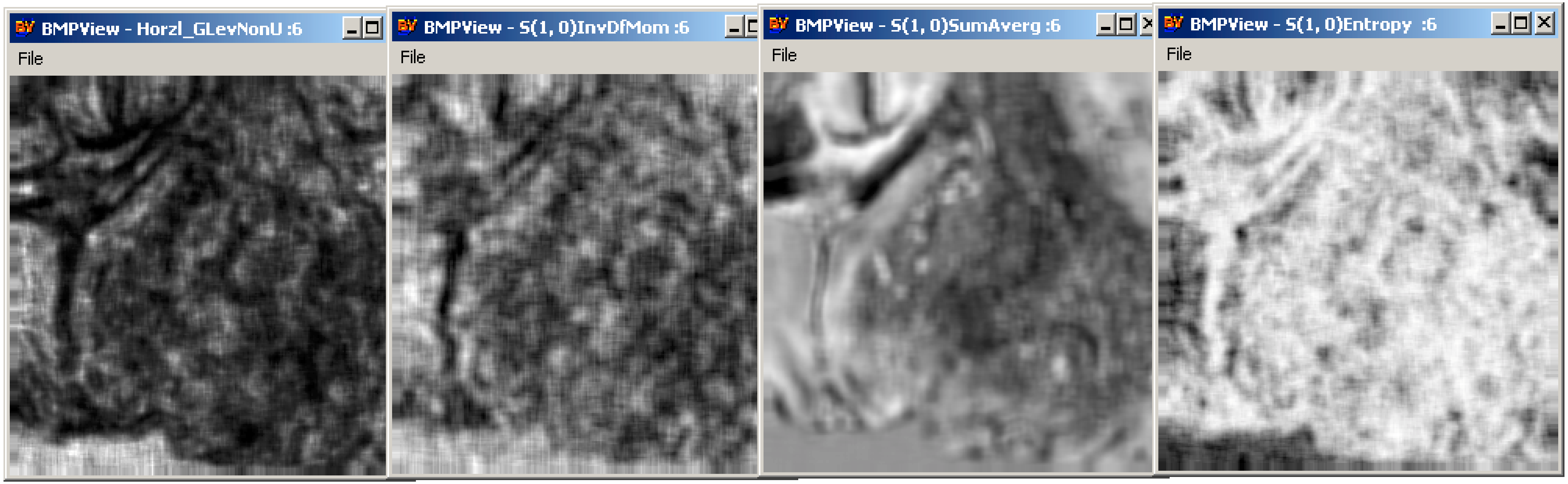
Textural features



Glioblastoma - textural features cont.



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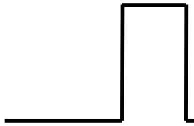
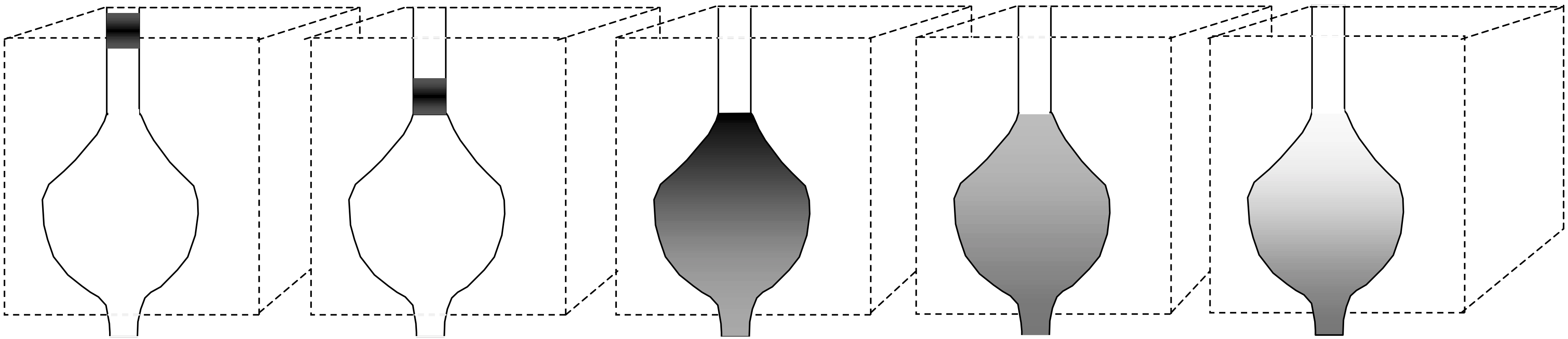
Physiological features

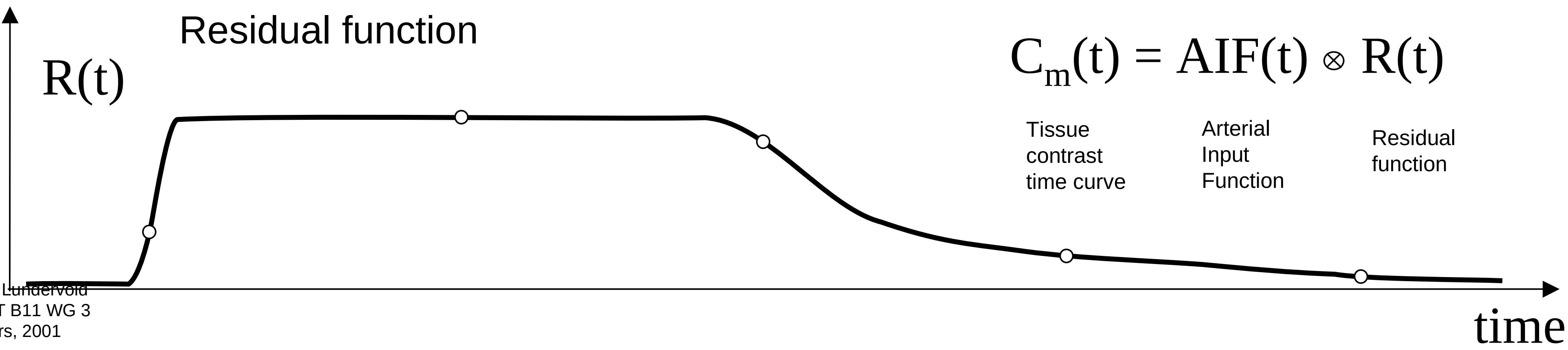


Impulse i.v. injection
of contrast agent

Wash in and wash out (or bolus passage) in capillary bed of brain tumor voxel



Residual function



$$C_m(t) = AIF(t) \otimes R(t)$$

Tissue contrast time curve	Arterial Input Function	Residual function

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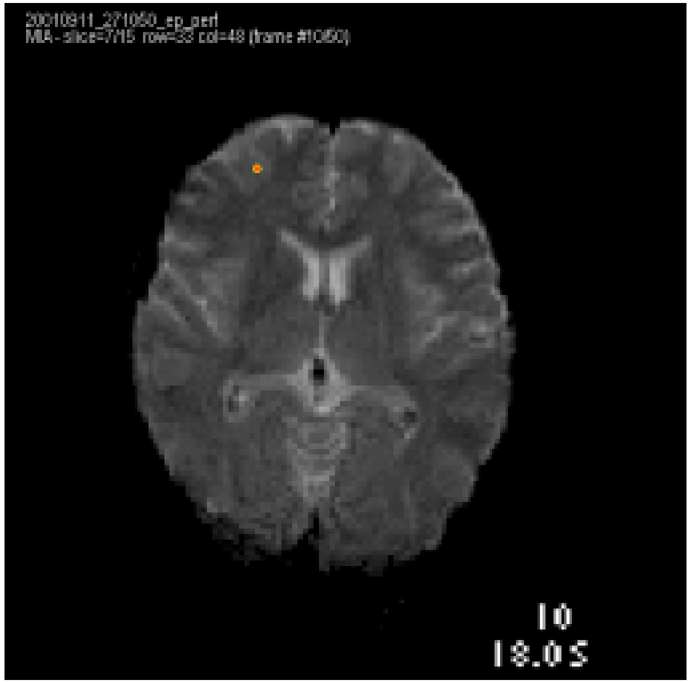
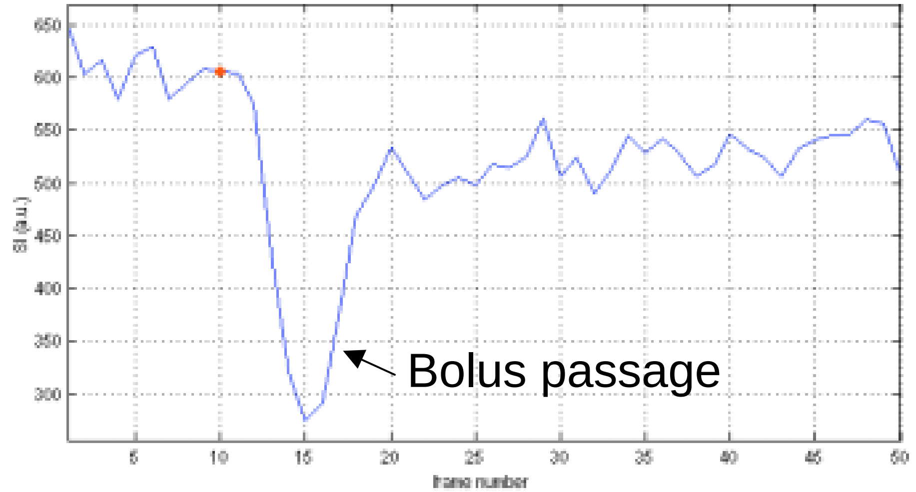
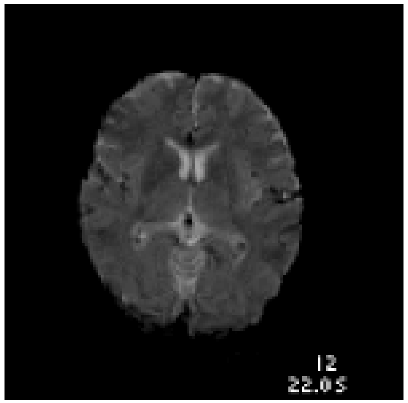
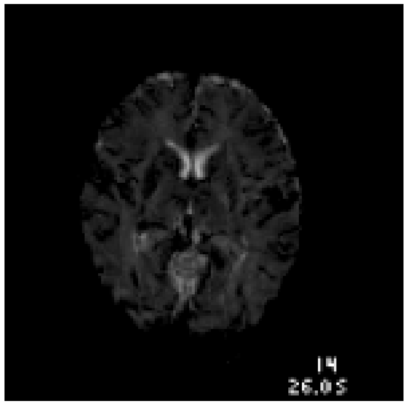
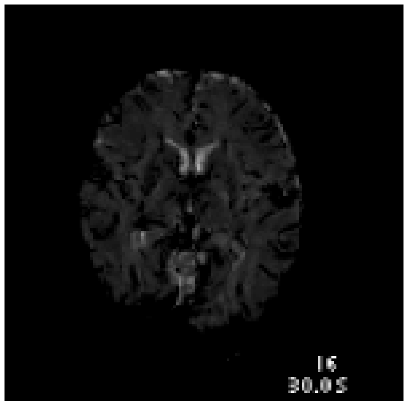
Signal intensity vs. time

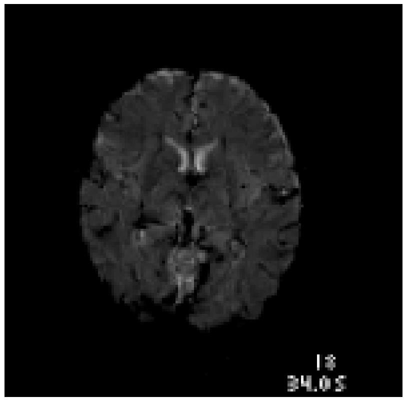


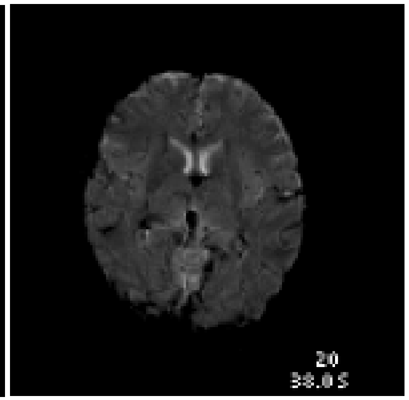












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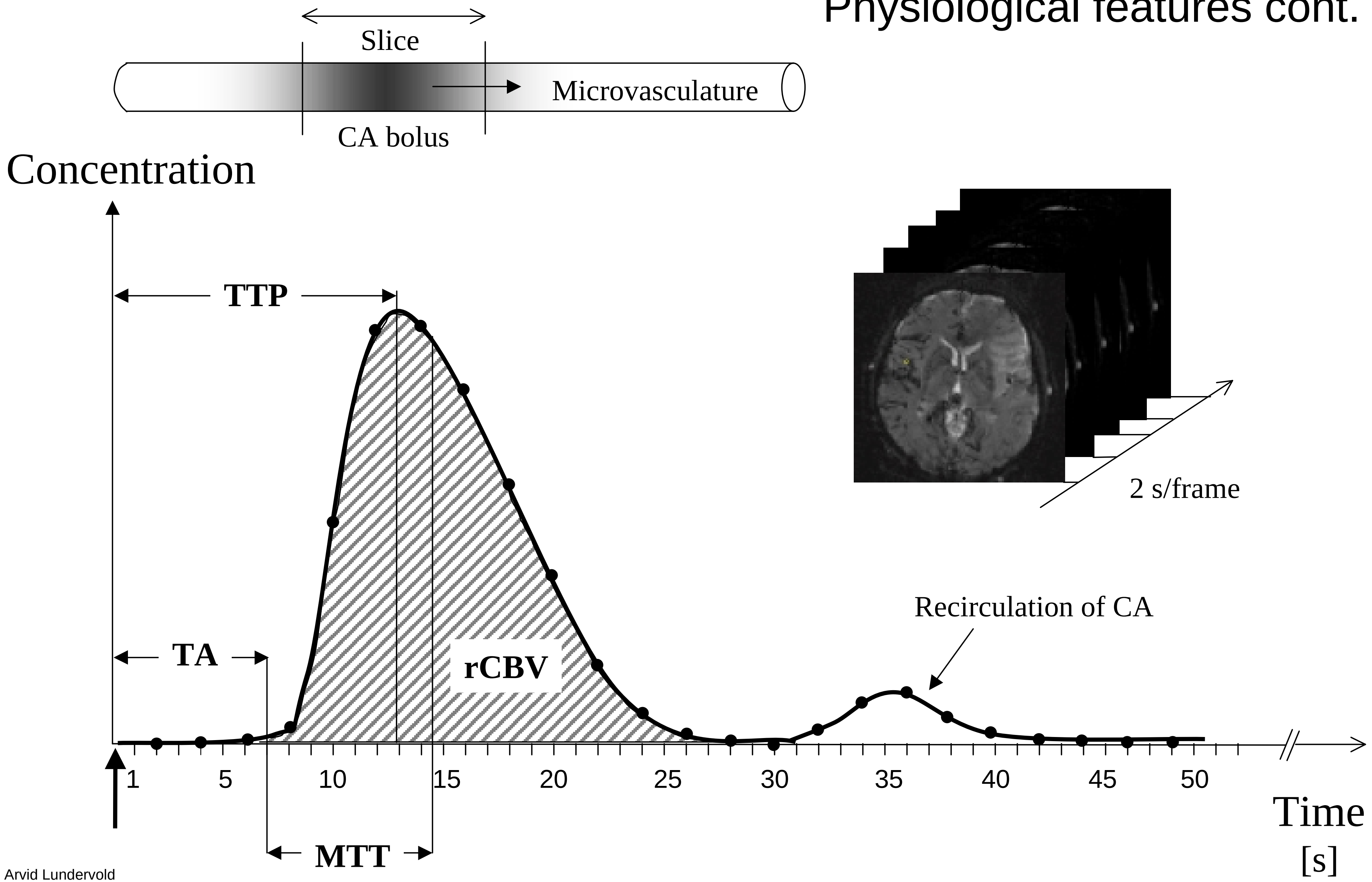
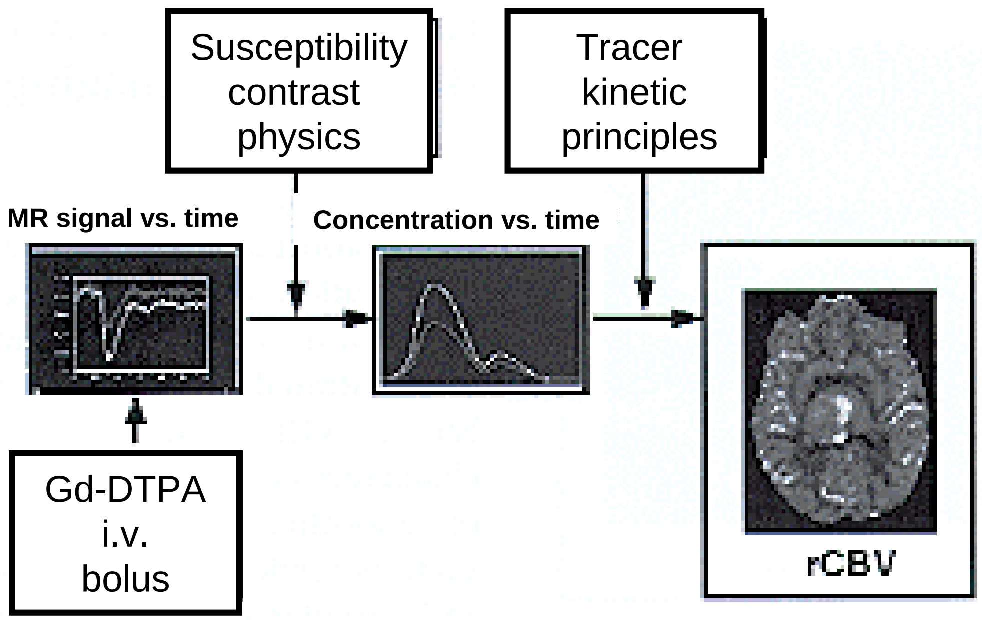
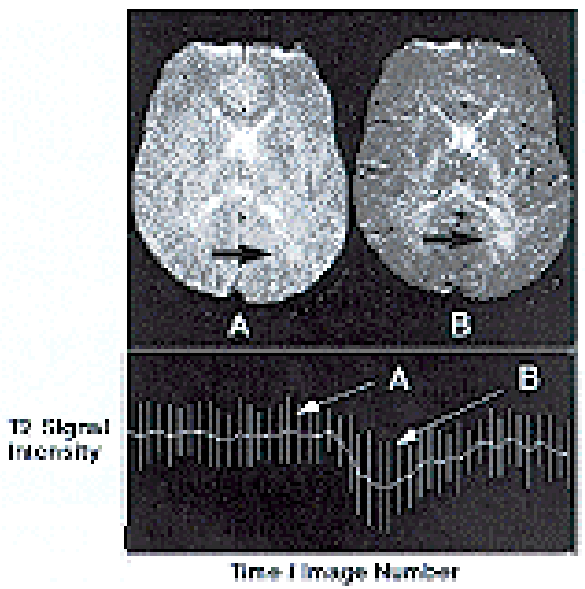
Physiological features cont.



“ Perfusion Magnetic Resonance Imaging to Assess Brain Tumor Responses to New Therapies “

From: Michael H. Lev, MD, and Fred Hochberg, MD





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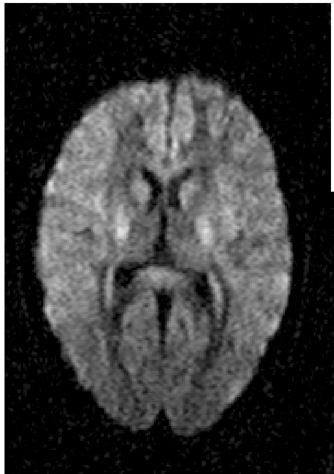
http://moffittcancercenter.org/pubs/ccj/v5n2/article2.html

Diffusion imaging



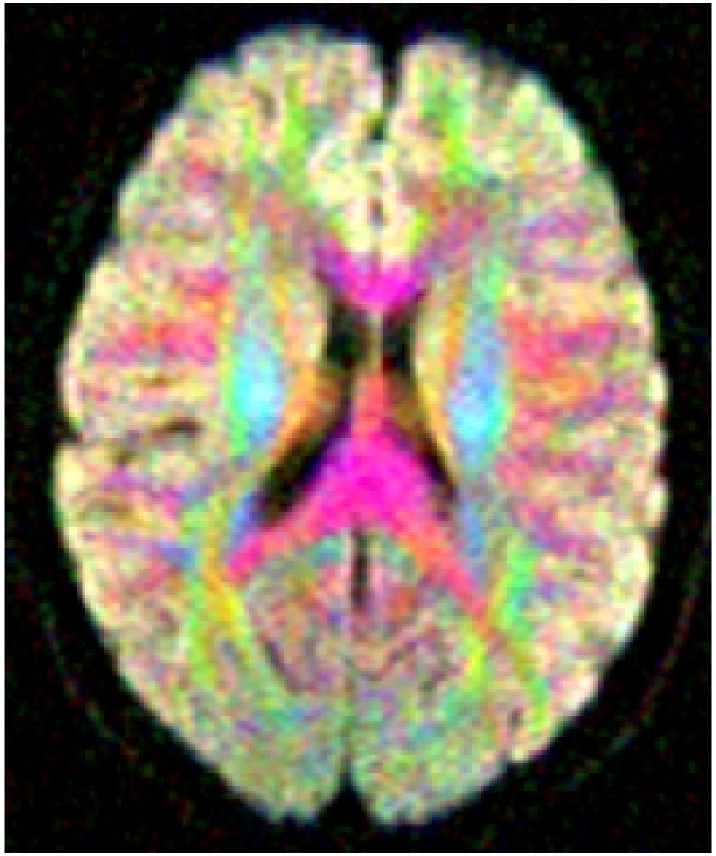
b=1000 P

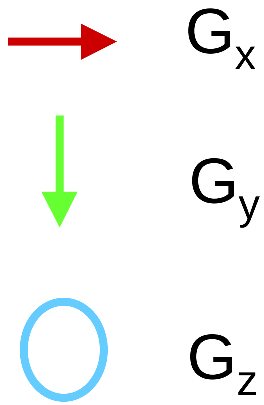
b=1000 R

b=1000 S

Siemens Vision

Color coding of the three orthogonal diffusion encoded images





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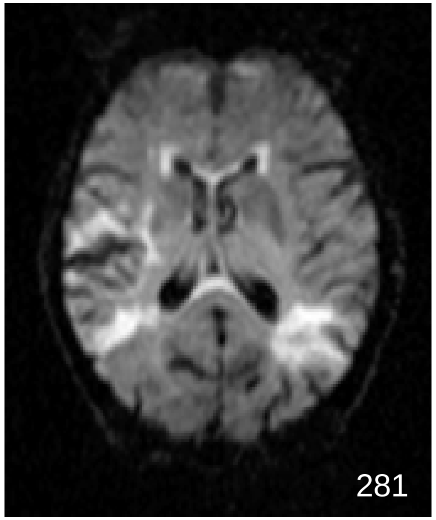
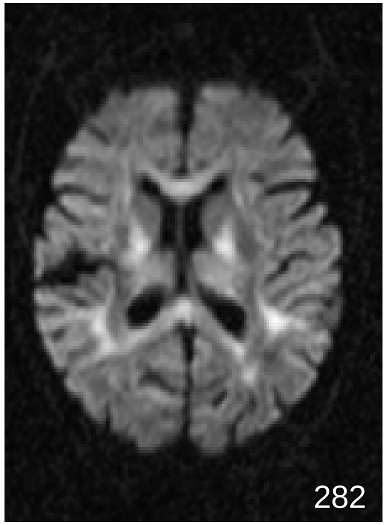
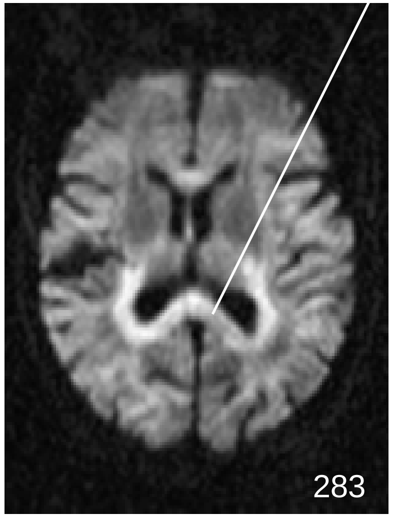
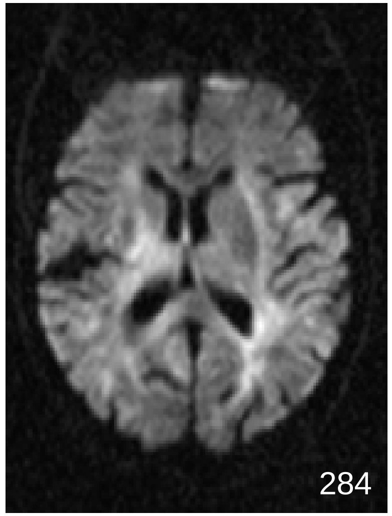
Diffusion Tensor Imaging (DTI)

Anisotropic diffusion of water
(corpus callosum)



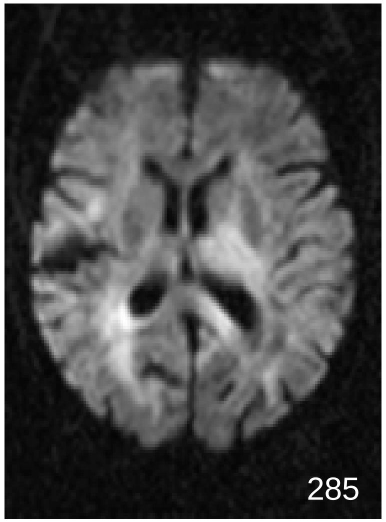


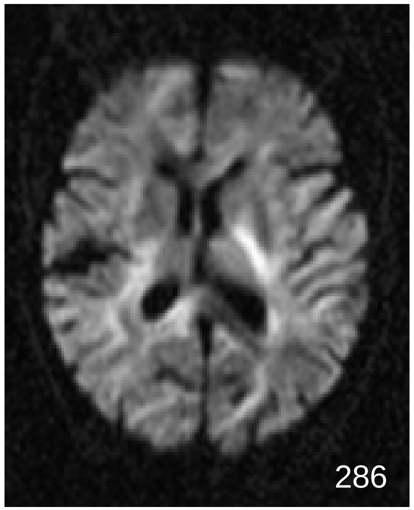


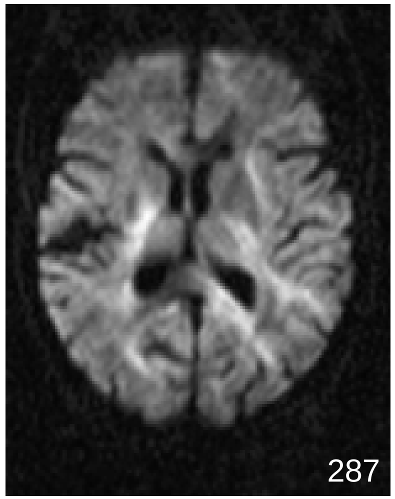


Diffusion tensor imaging of a 75 year old woman with stroke.
b=1000 s/mm^2 in 6 different directions.
The diffusion tensor FLAIR sequence (ep2d_ir_dt6_2_ic_4aq.ek) was written by Dr. Jochen Hirsch at Klinikum Mannheim on a Siemens Vision. TA= min 42 s, 4 AC;
Matrix=128 x 200, TR=6000 ms;
TE=110 ms; TI=1950 ms;
Thickness=5 mm; FOV=240 x 240 mm^2

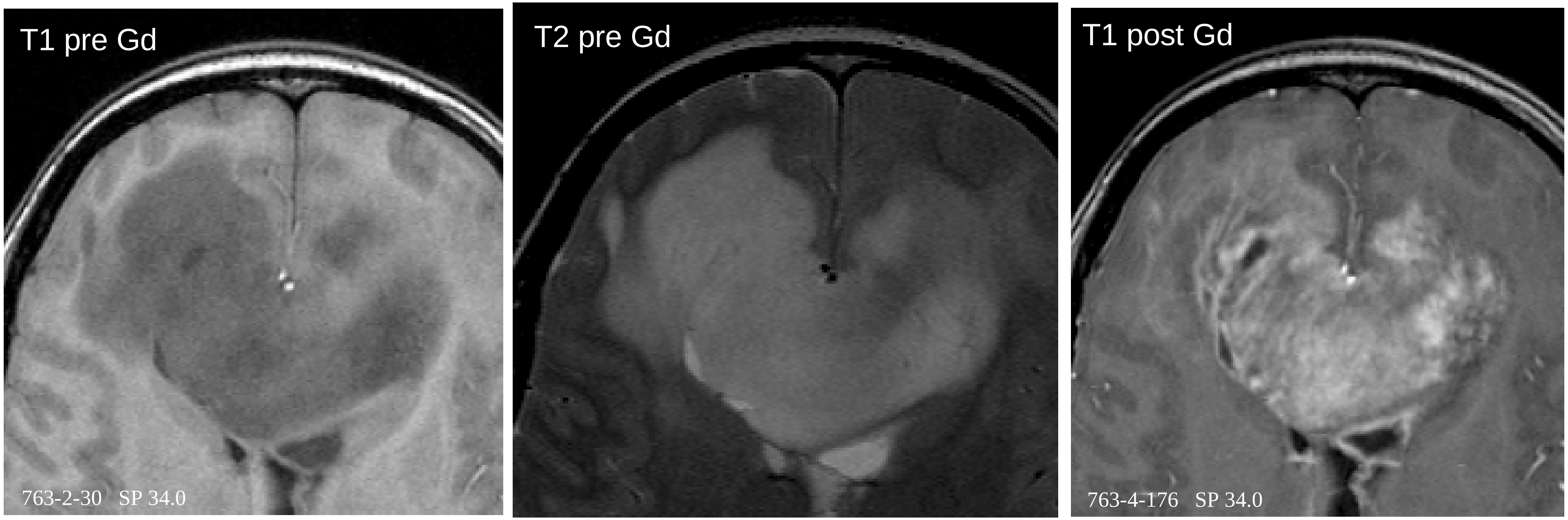
(Courtesy of Prof. L. Schad, DKFZ, Heidelberg)







Multispectral imaging of glioblastoma (DKFZ)



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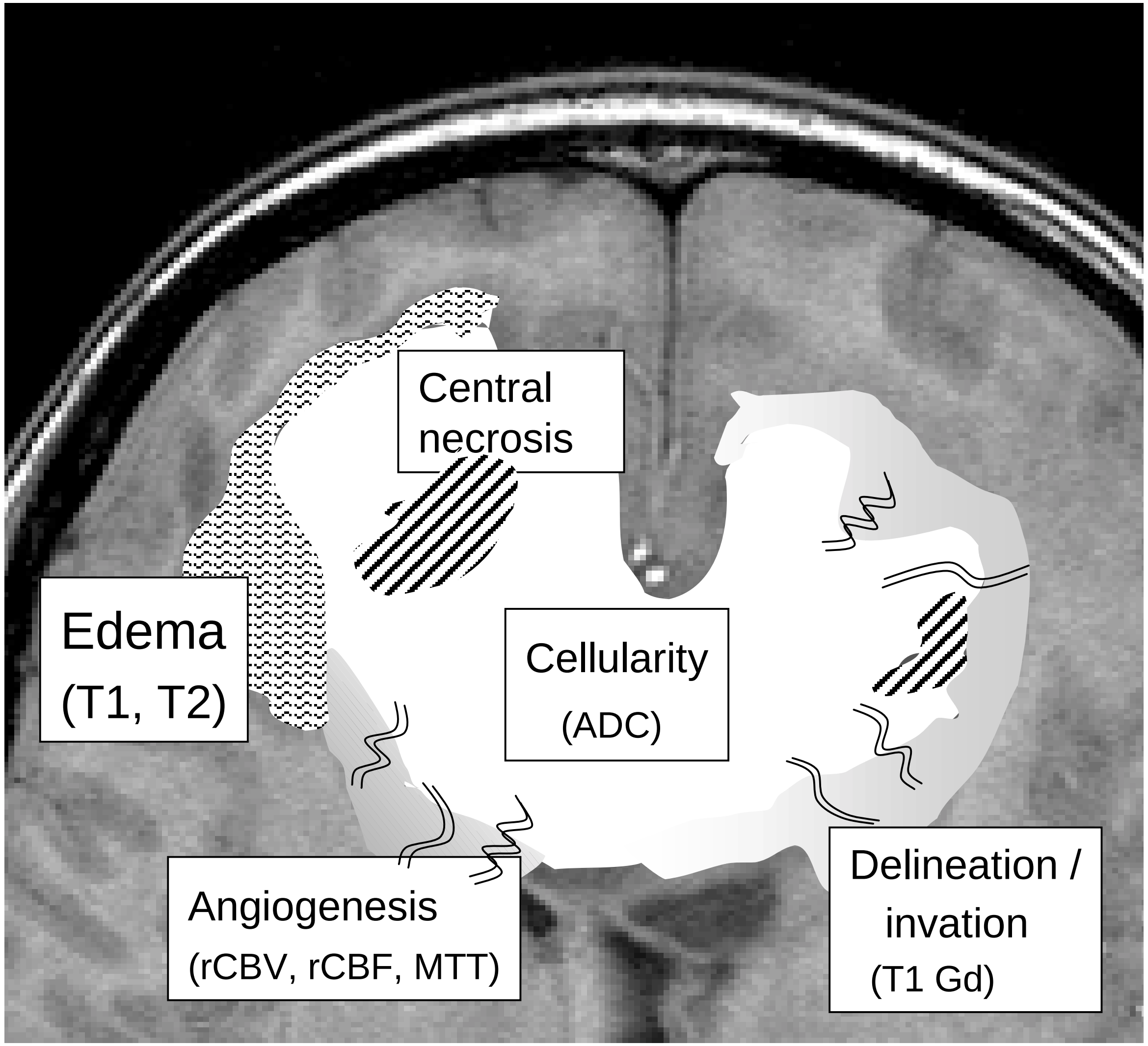
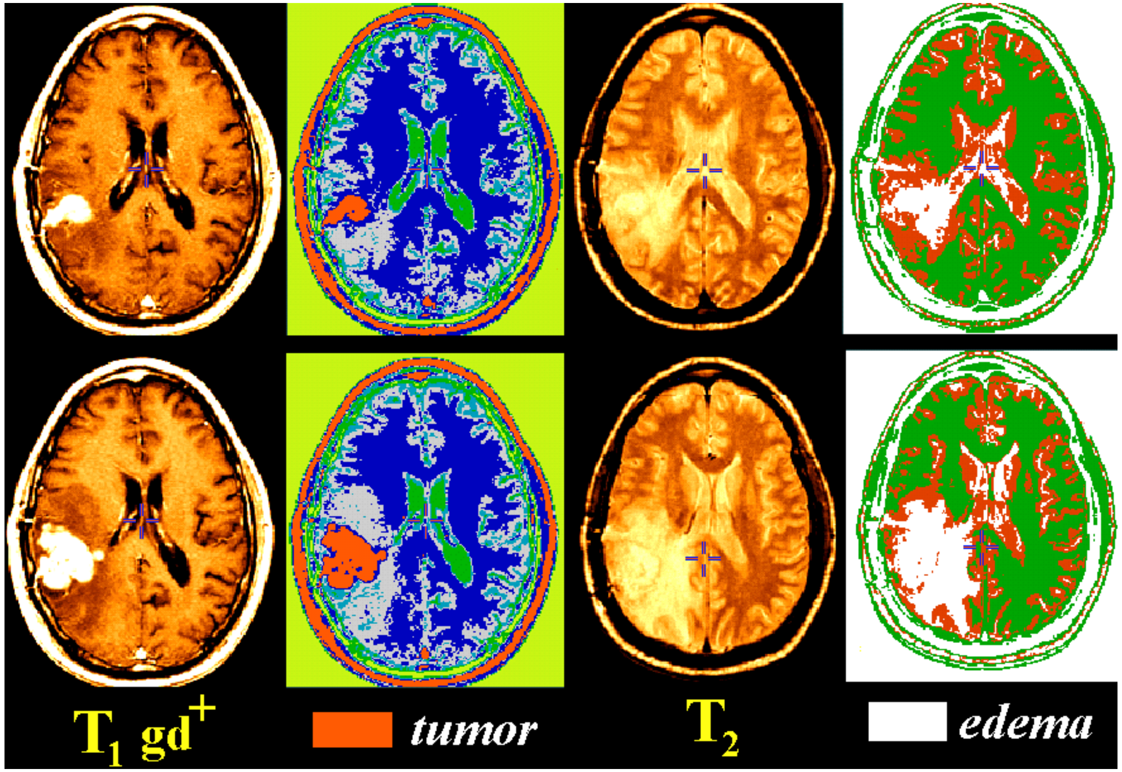
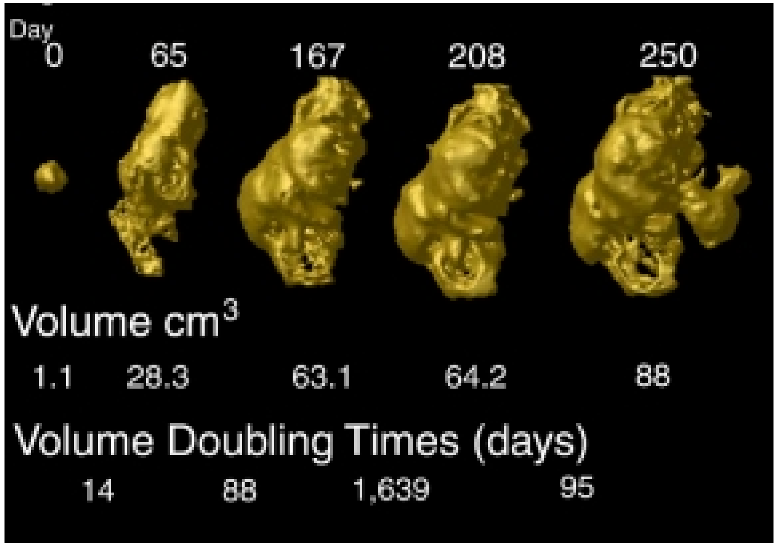
Tissue anatomical and physiololgical features



Tissue classification of normal and abnormal tissue types from multispectral MR image acquisitions in GBM patients

- assessment of tumor growth rates and response to therapy





Growth Rates, MR Spectroscopy: Prognostic Markers for Glioblastoma Multiforme

Society for Neuro-Oncology, Chicago, Nov. 2000

Haney S, Thompson PM, Cloughesy TF, Alger JR, Frew AJ, Toga AW
Laboratory of Neuro Imaging, Department of Neurology, Division of Brain Mapping; Neuro-Oncology Program, The Henry E. Singleton Brain Cancer Research Program; Dept. of Radiological Sciences; UCLA School of Medicine, Los Angeles, CA 90095

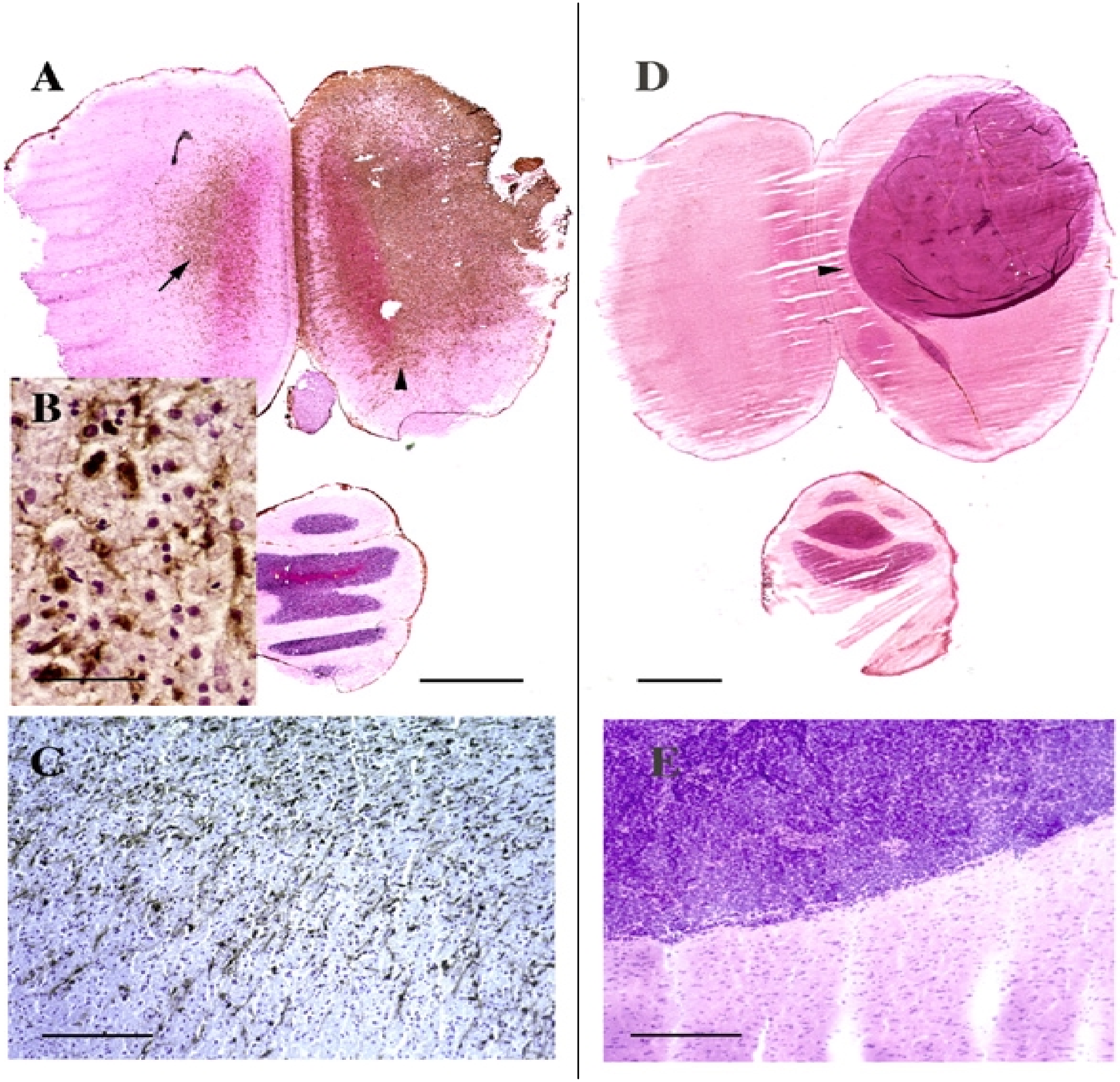
http://www.loni.ucla.edu/~thompson/scottsdale99.html

Experimental brain tumors in the rat

Data from Prof. Rolf Bjerkvig,
University of Bergen

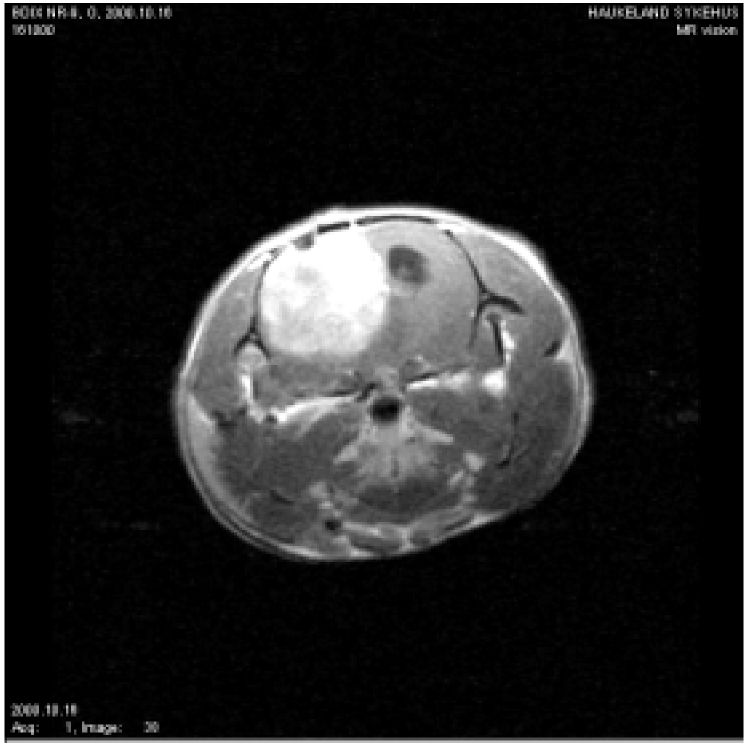
A-C Human xenograft in nude rats demonstrating tumor cell infiltration in brain parenchyma.

D & **E**. Human tumor obtained by implantation of a permanent human glioma cell line.
Tumor growth is here by expansion rather than by infiltration, and image texture in the micrographs have different characteristics.



Imaging of tumor growth in the rat brain

using the finger coil on a 1.5 T Siemens Vision



lp-loop-small/t1_se_sag,   se_14b89.ykc
250 gr 0.5 ml Gd ,   TA=4:59,   AC=3
Matrix=224*256os,   TR/TE=440.0/14.0 SL=2.0
FoV=44*50   Voxel size = 0.20 x 0.20 x 2.0 mm^3

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Rat brain imaging on a clinical whole-body scanner

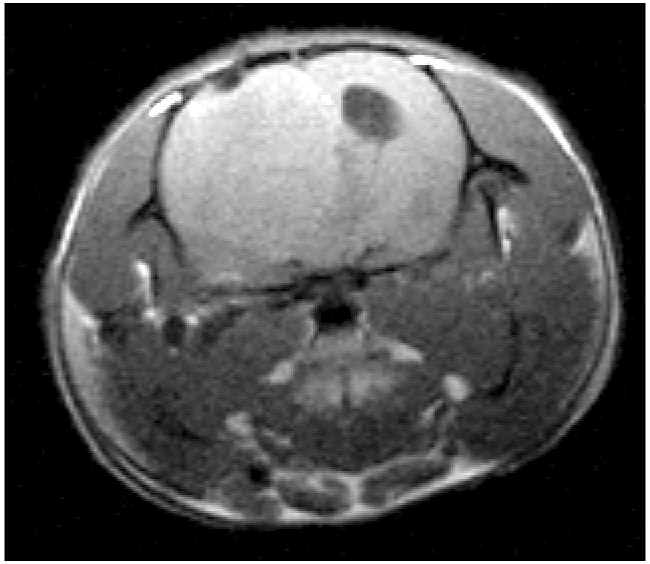


Image 3-12 (T1)
TR/TE = 440/14

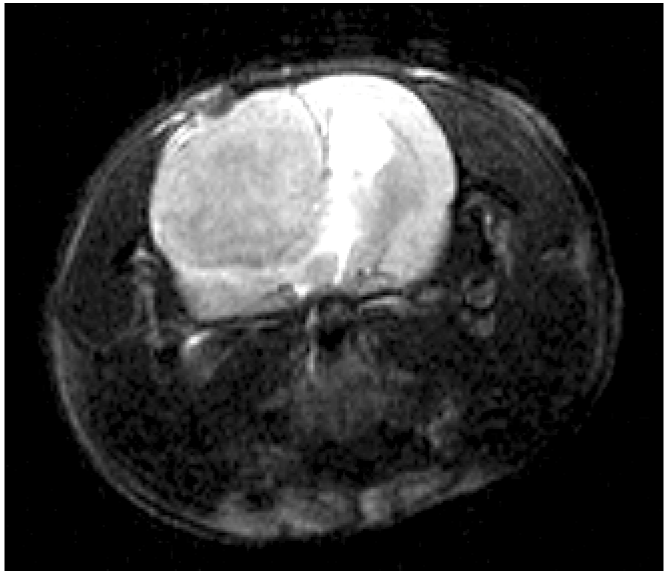


Image 4-25 (T2)
TR/TE = 4000/96

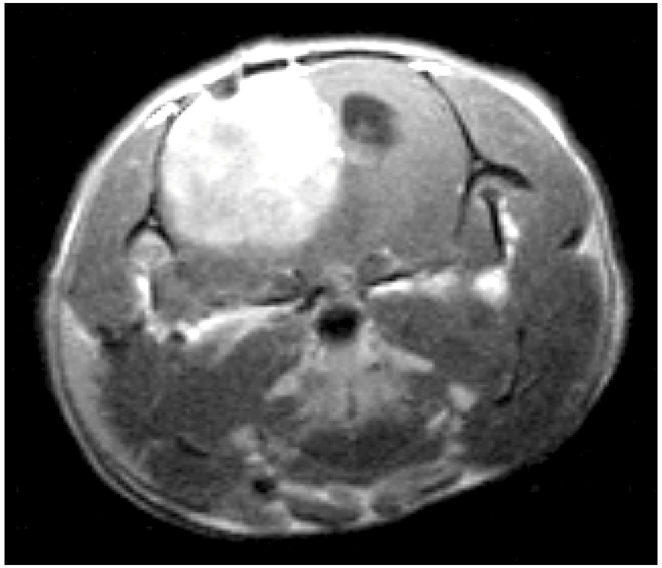


Image 5-38 (T1 Gd)
TR/TE = 440/14

se_14b89.ykc

Texture analysis in multispectral images of human glioblastoma acquired at DKFZ (study 763)

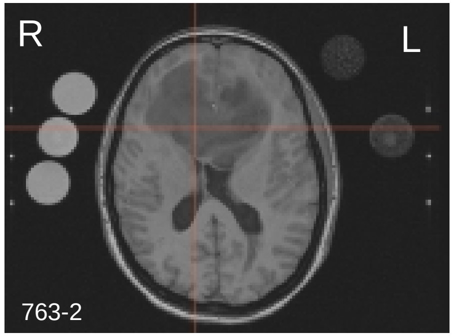
Phantoms

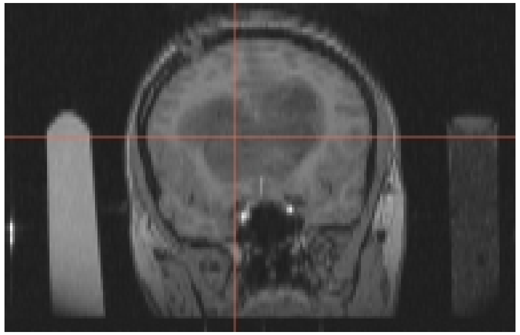
R: Reticulated foam
- coarse
- empty
- medium

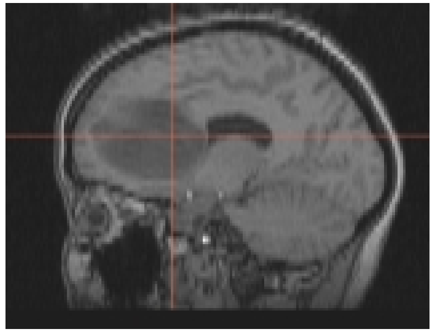
L: Polystyrene granules
- 2.00 - 3.15
- 1.25 - 2.00
- 0.80 - 1.25

F 48 Y

SIEMENS VISION 1.5 T







Pre (763-2-) **and post** (763-4-) **Gd:**

Sequence = fl3dt1_fe34_476rb97.ykc

TR/TE/FA = 20.1/6.5/25° Acq = 1

Matrix = 384 x 512_{os} x 56 slices

FoV = 270 x 270

Voxel size = 0.70 x 0.53 x 3.0 mm^3

TA = 7 min 15 sec

Pre (763-3-) **Gd:**

Sequence = tse5_14b130_85b130.wkc

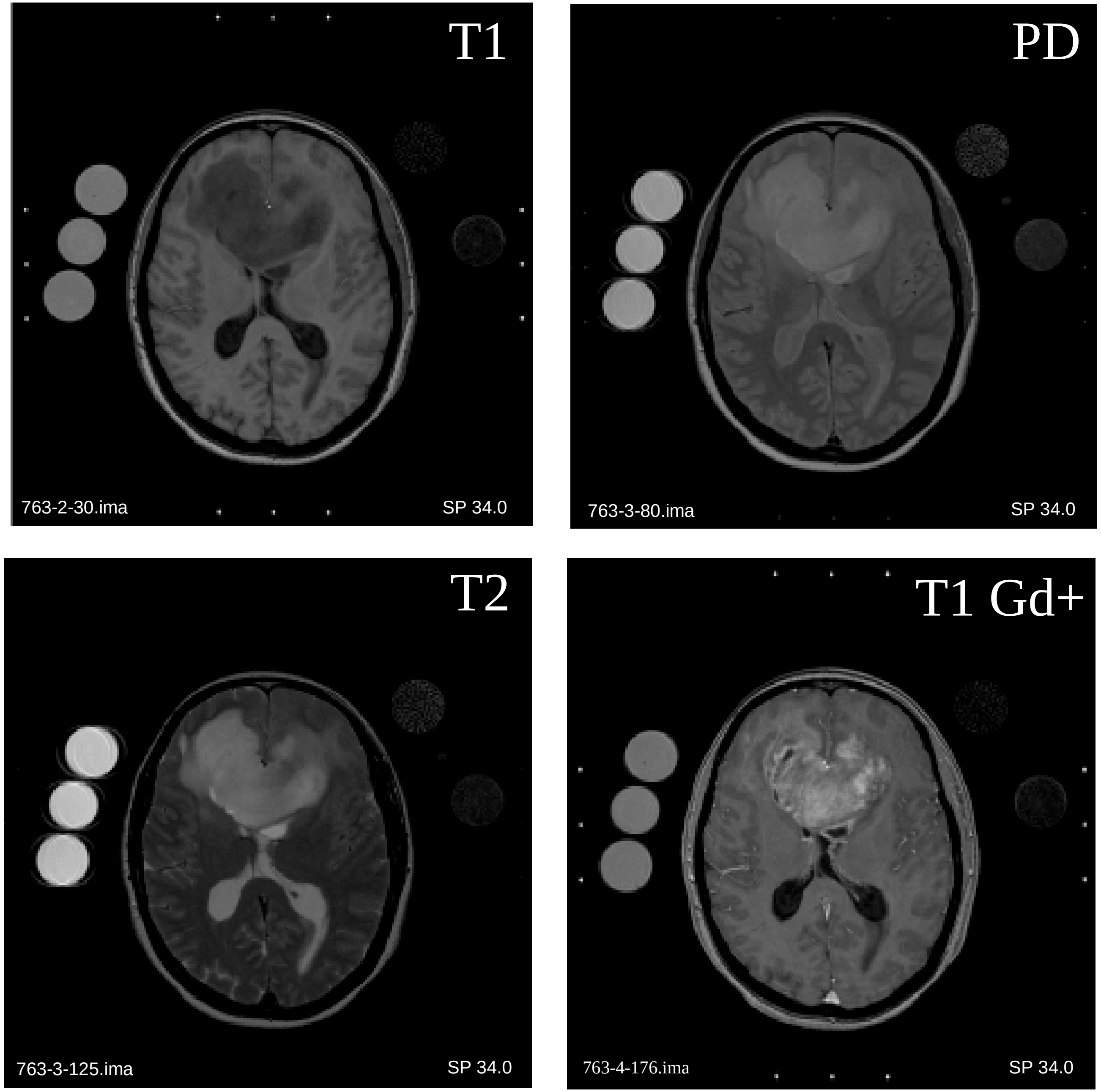
TR/TE1/TE2 = 5000.0/14.0/85.0 Acq = 1

Matrix = 340 x 512_{os} x 45 slices

FoV = 270 x 270

Voxel size = 0.79 x 0.53 x 3.0 mm^3

TA = 5 min 46 sec



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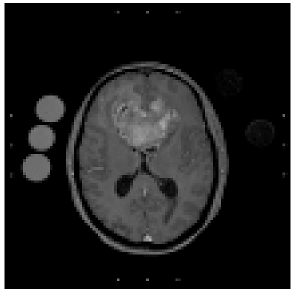
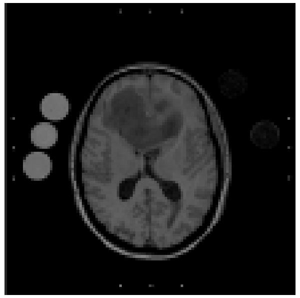


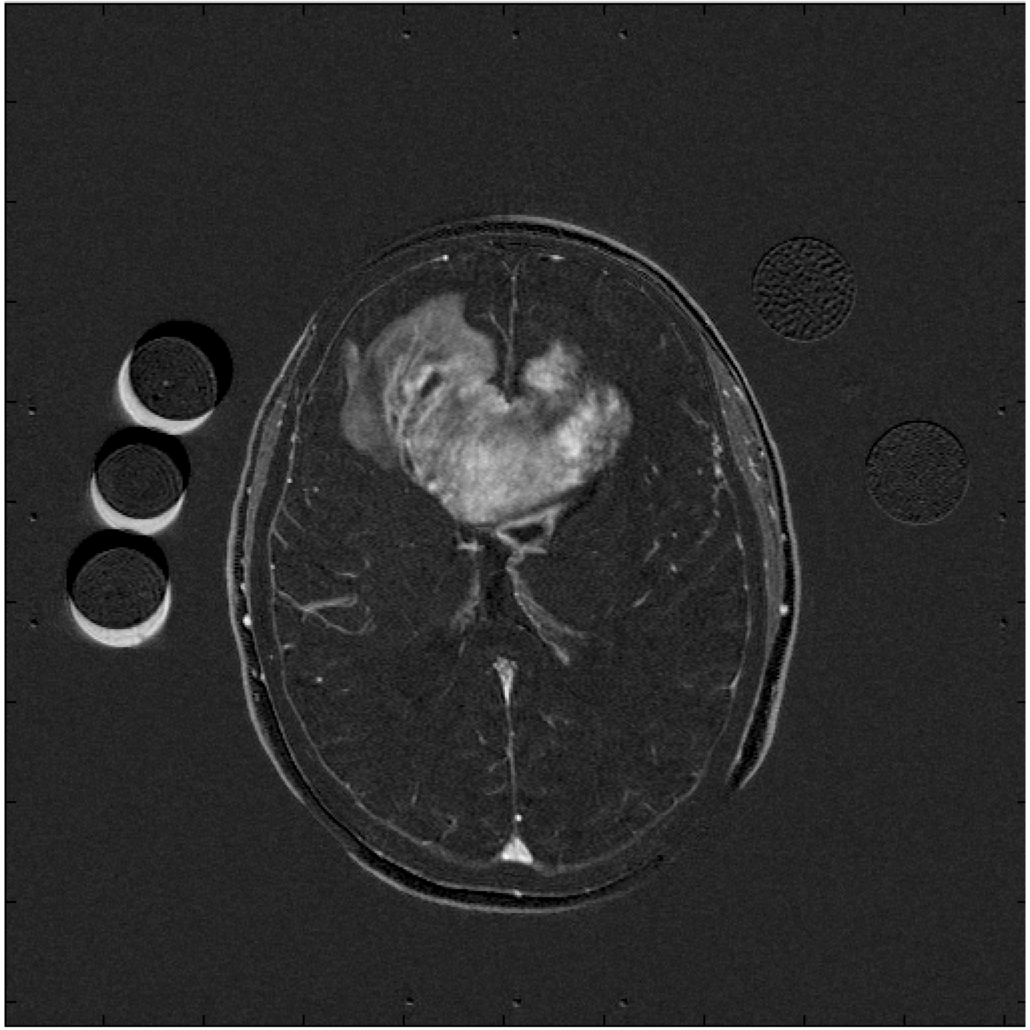
Post Gd
(12:36)

-



Pre Gd
(12:51)

=



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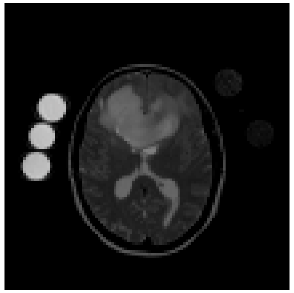
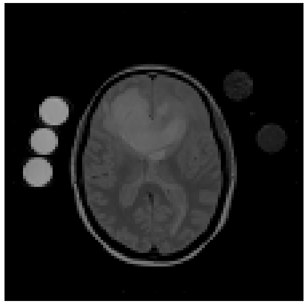


T2
(12:44)

-



PD
(12:44)

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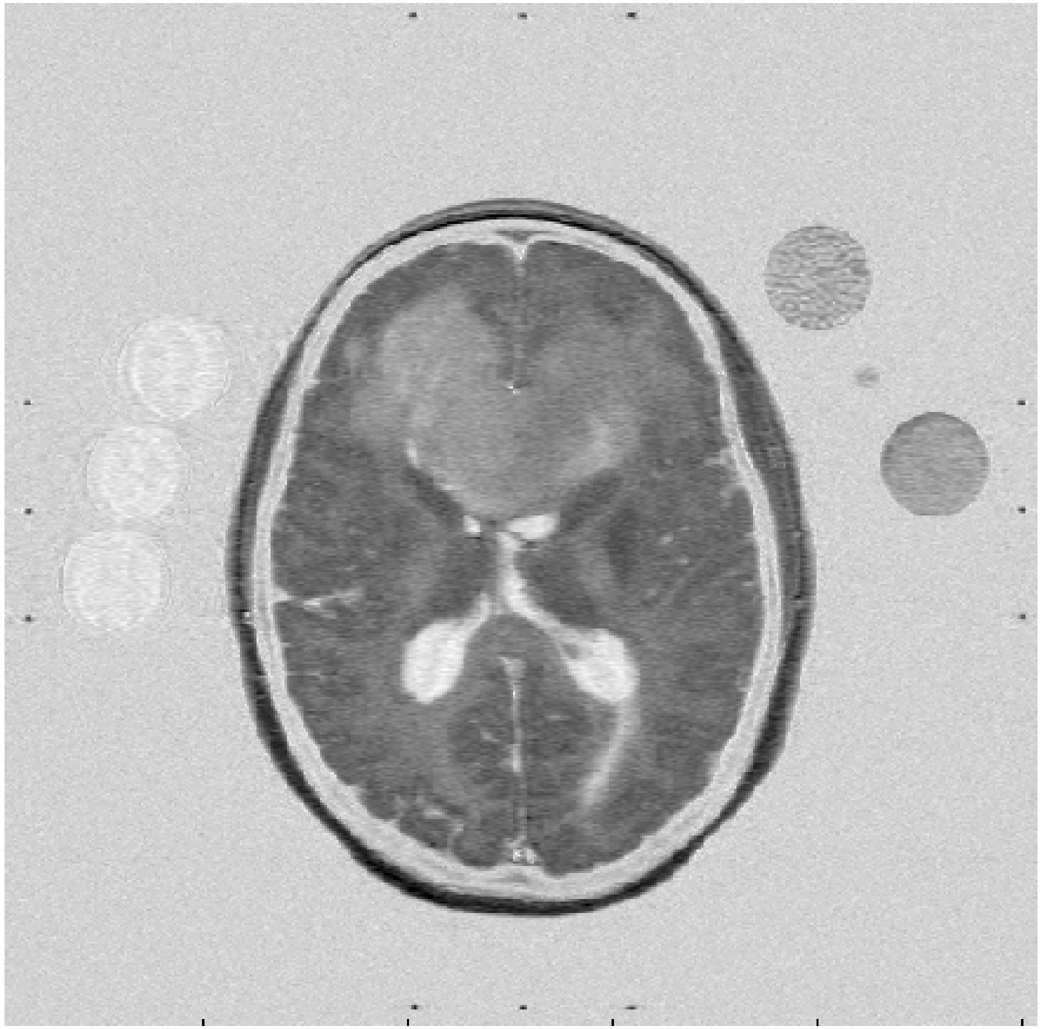

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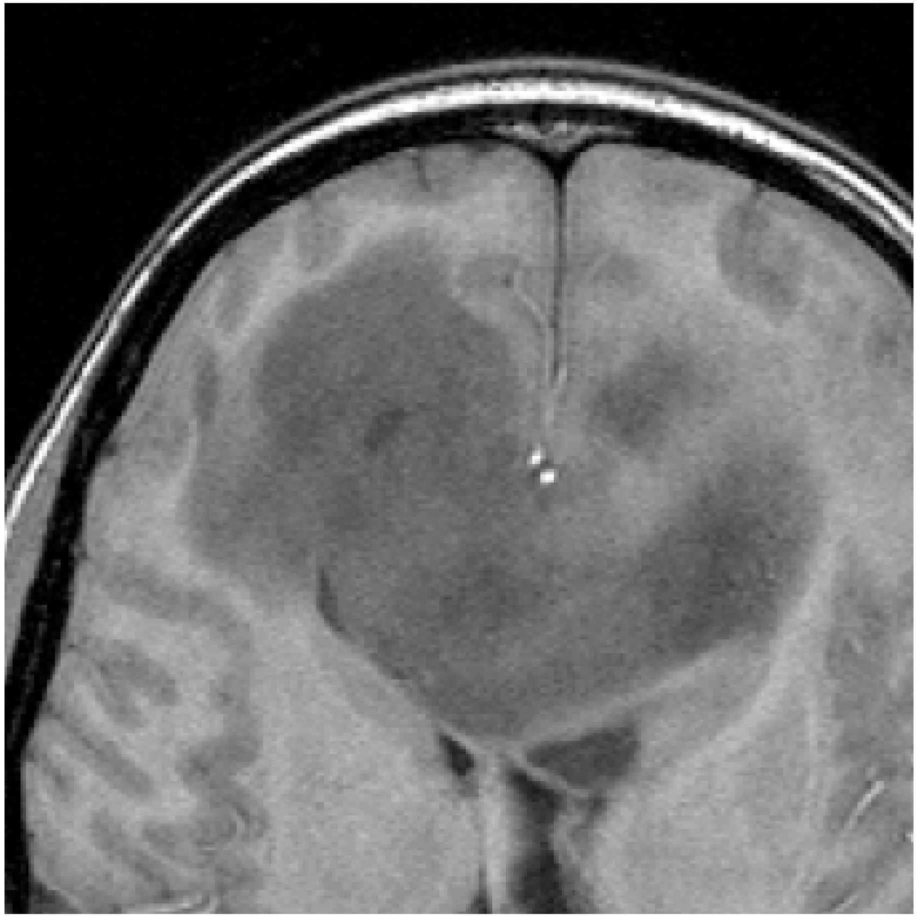

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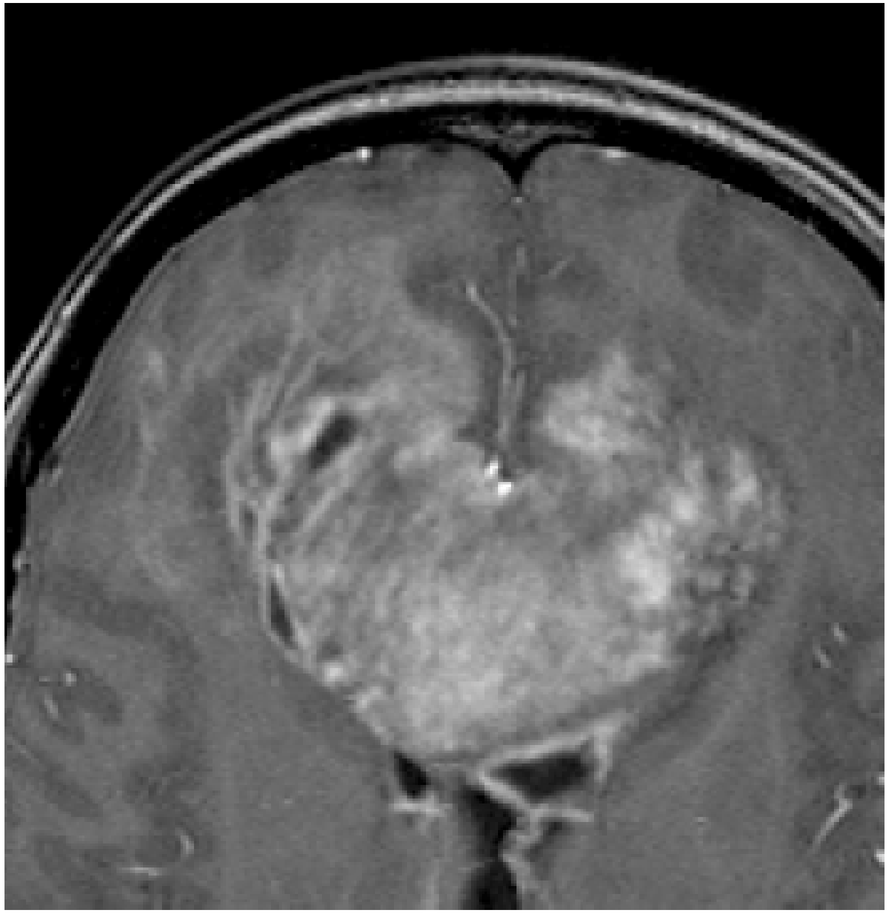

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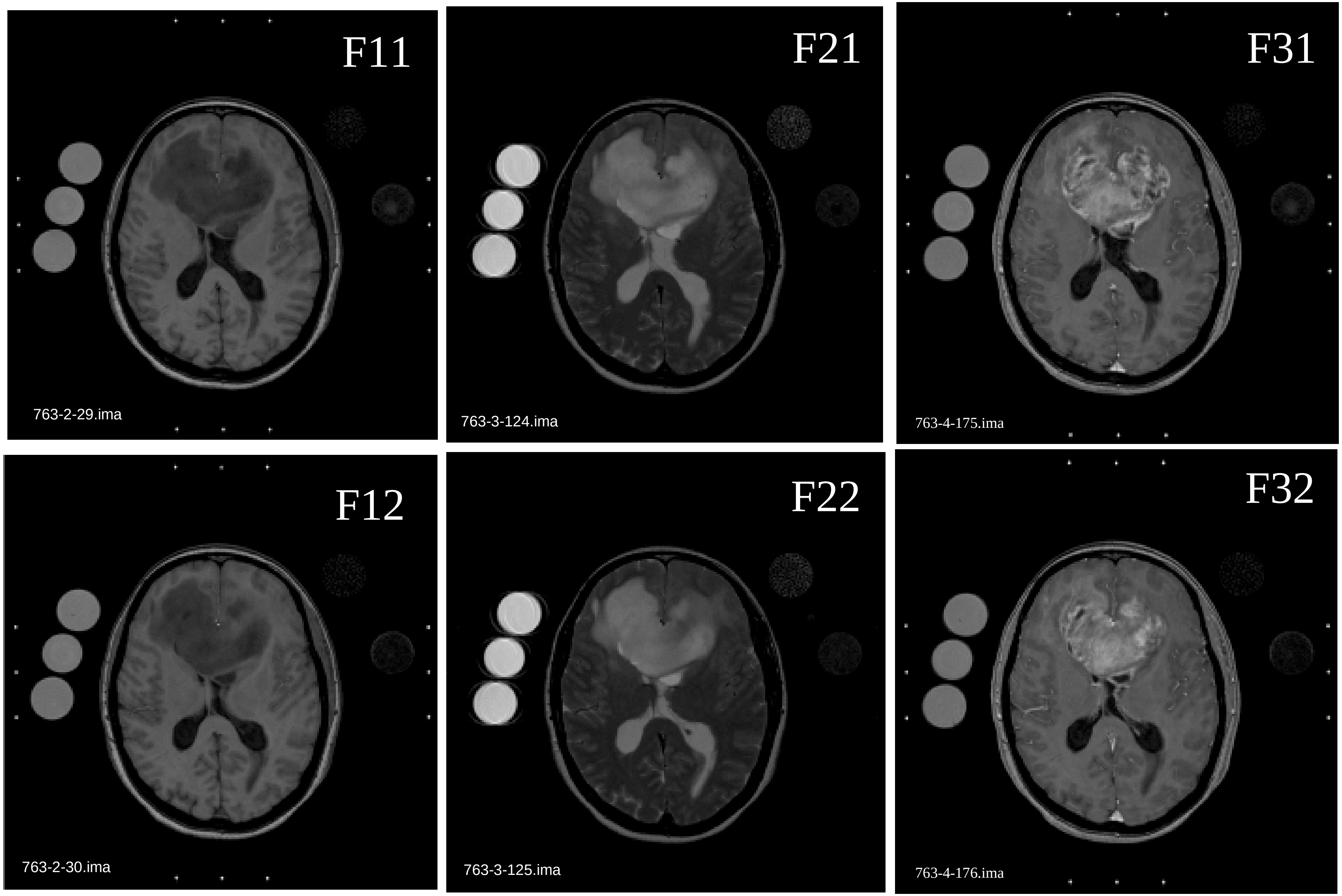

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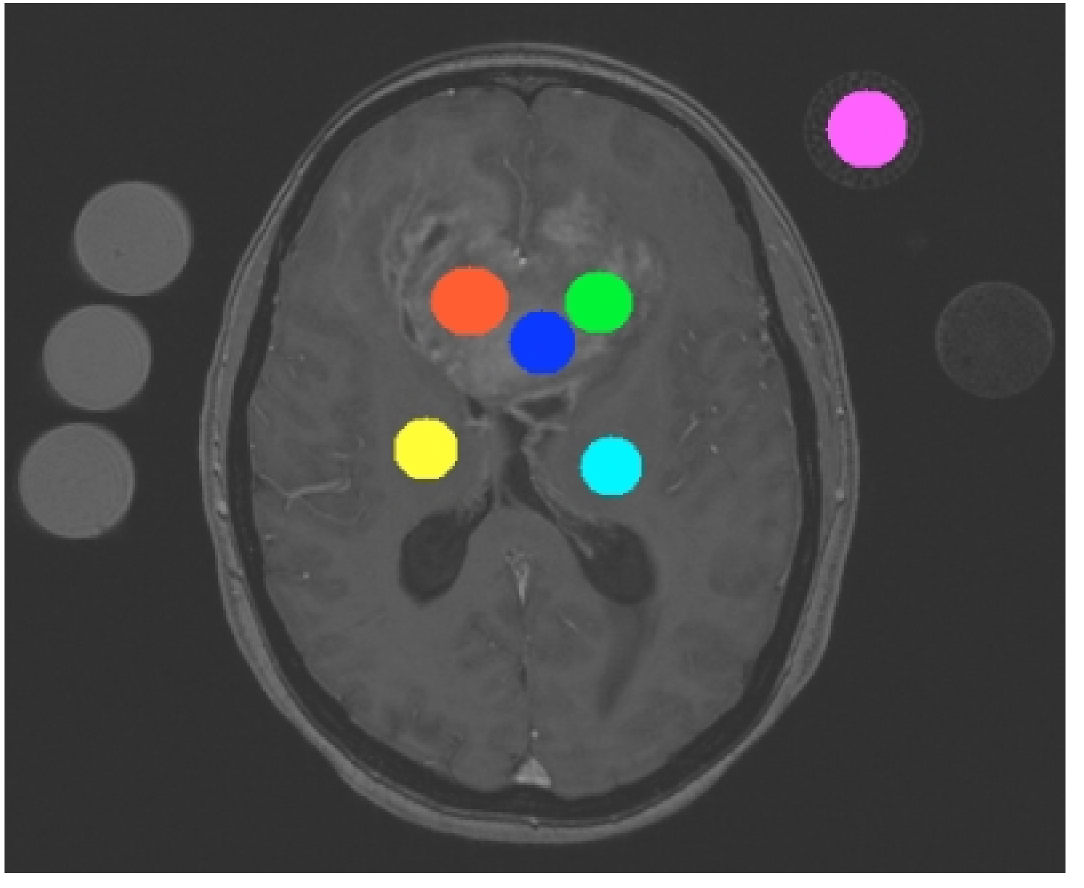
tumor3_wm2_phant1_roi.bmp



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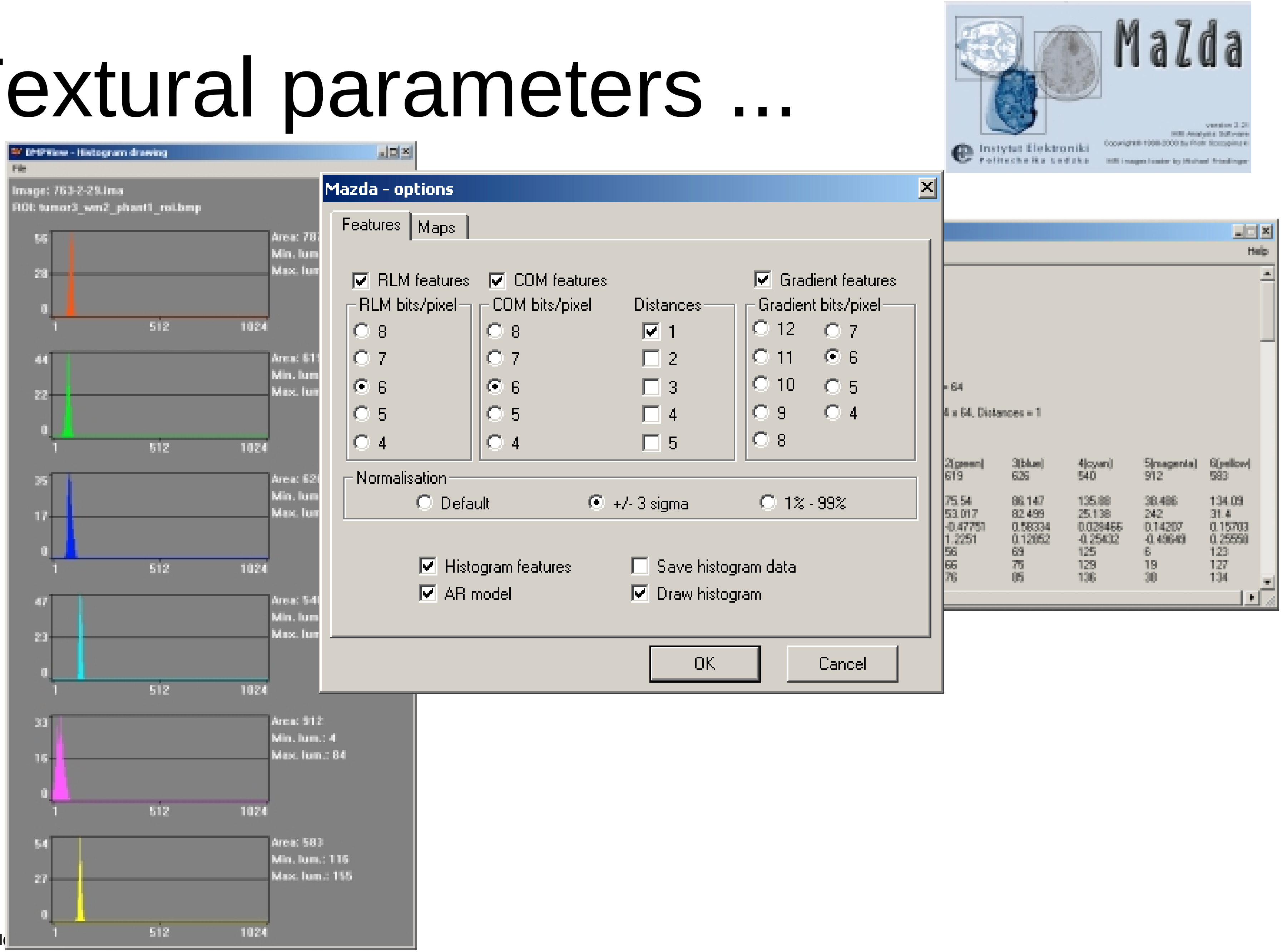
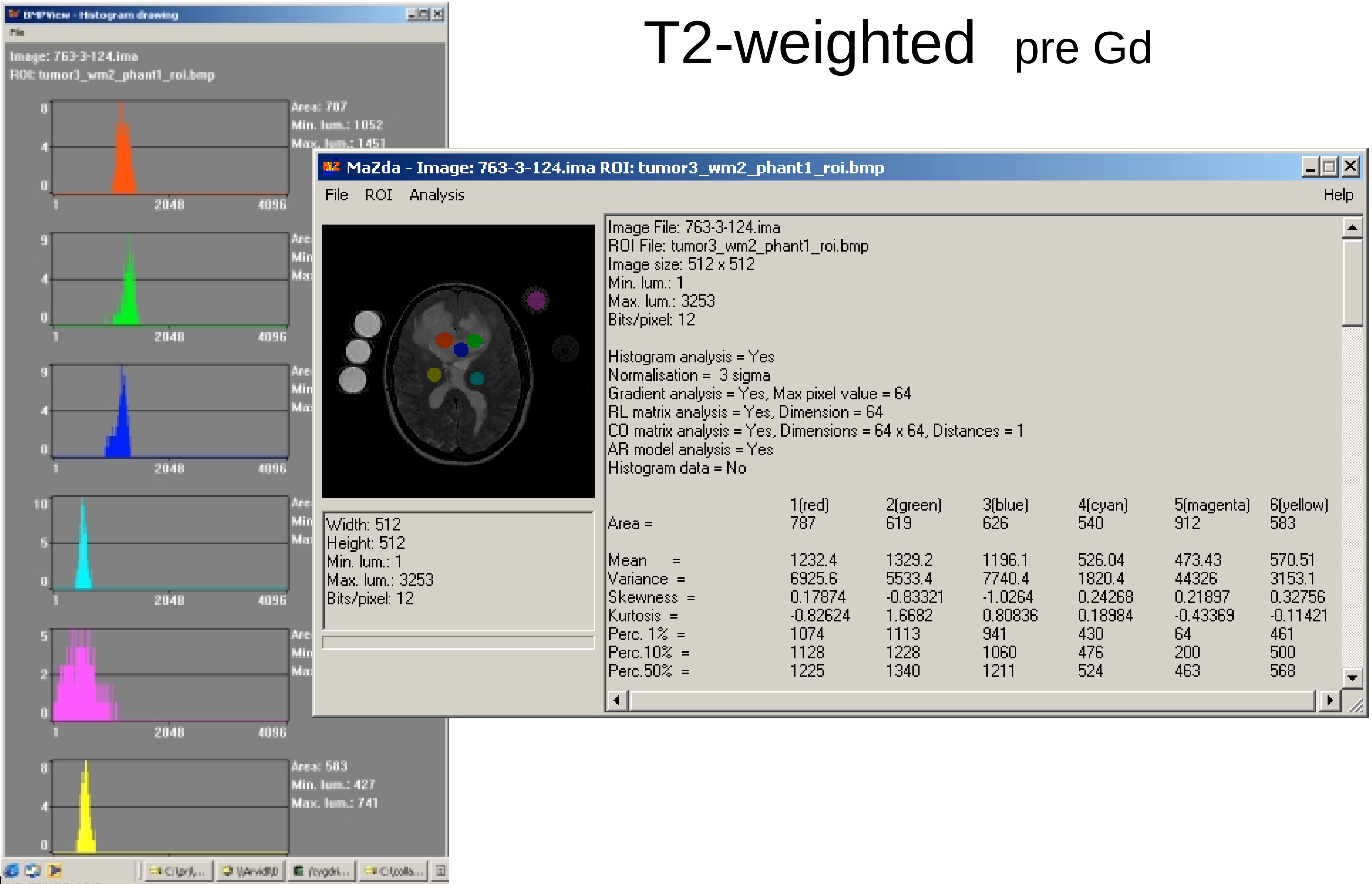
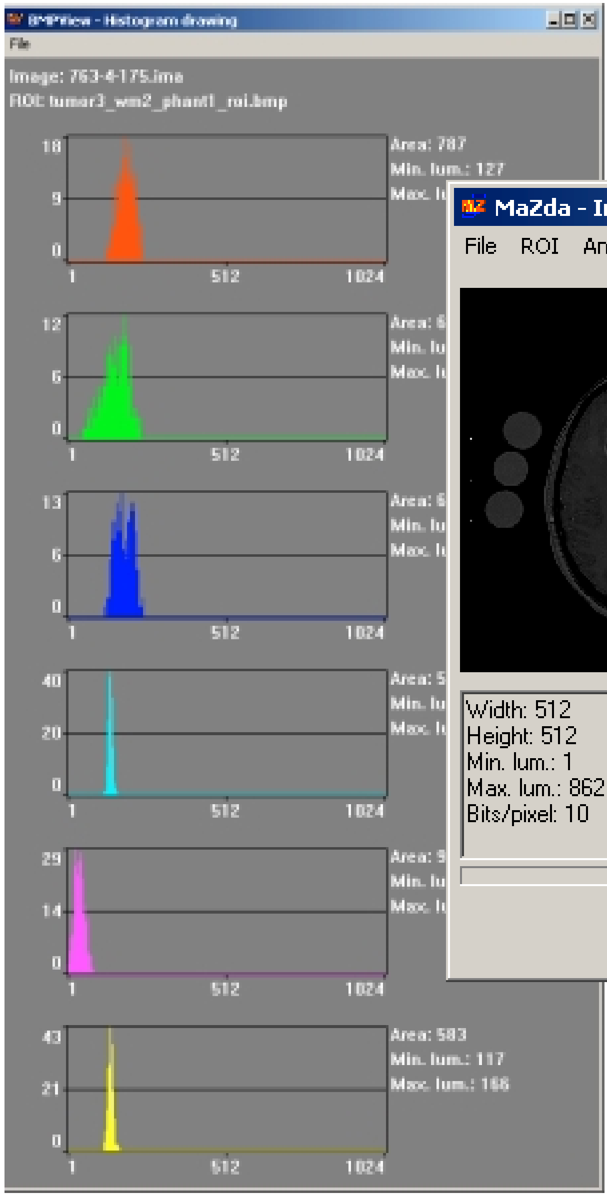
Textural parameters ...

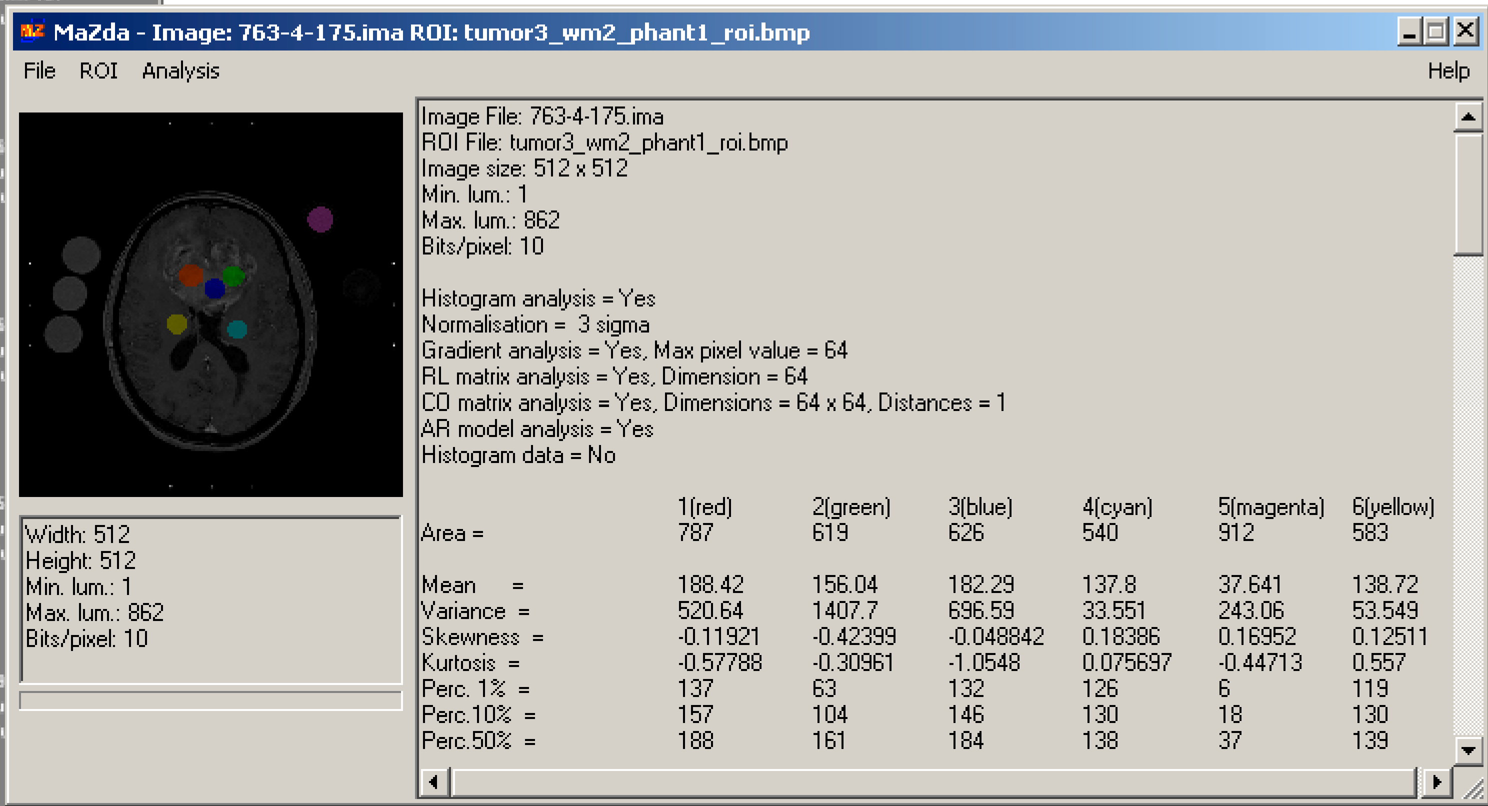


T2-weighted pre Gd



T1-weighted post Gd





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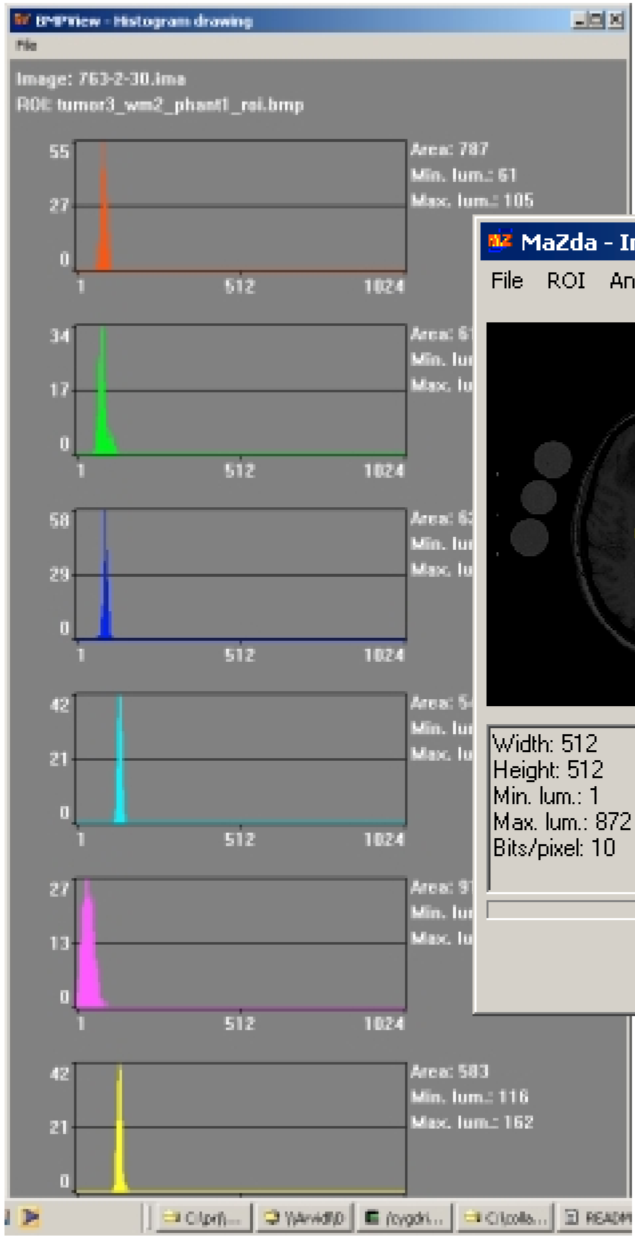
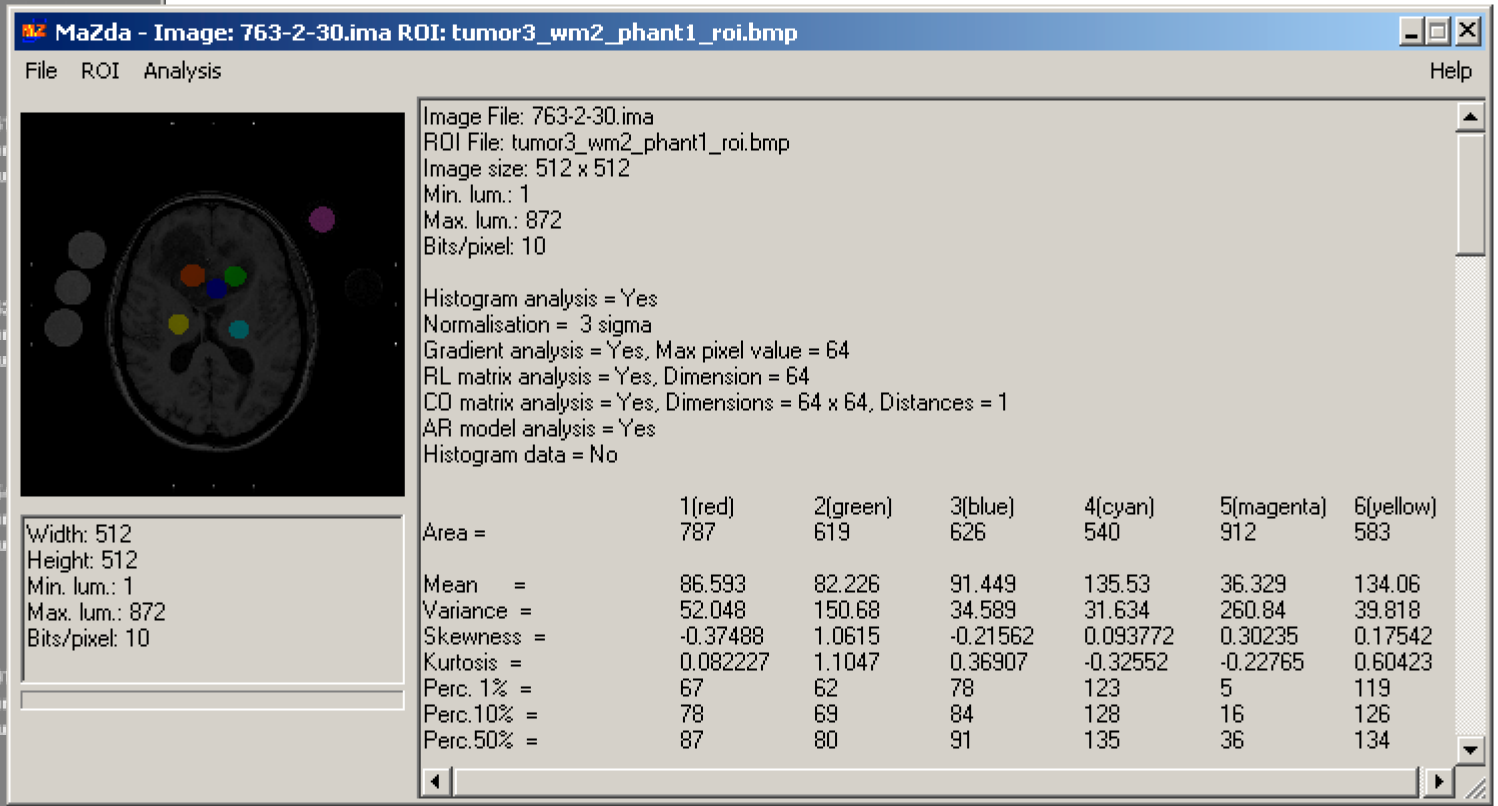
T1-weighted pre Gd





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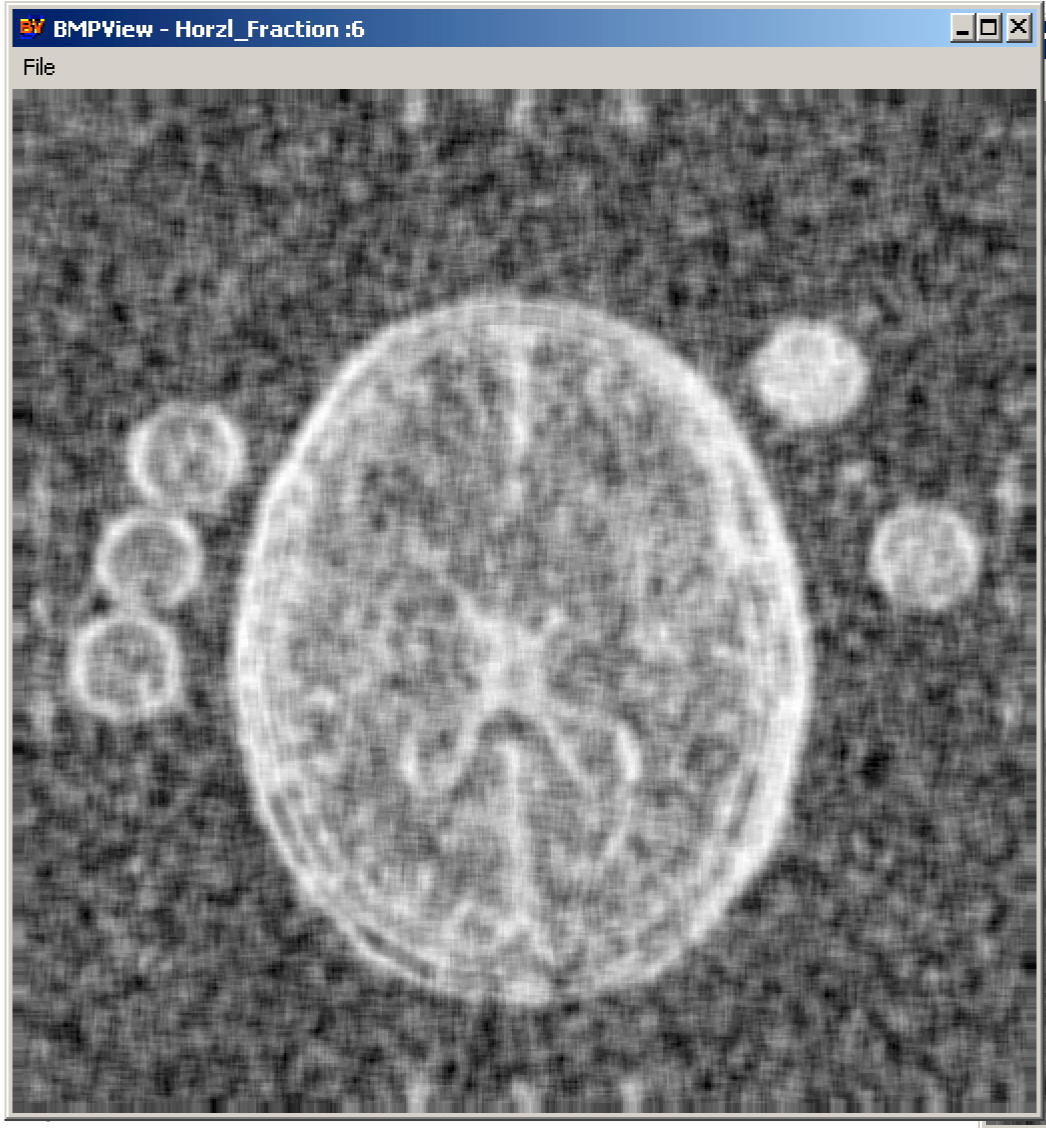
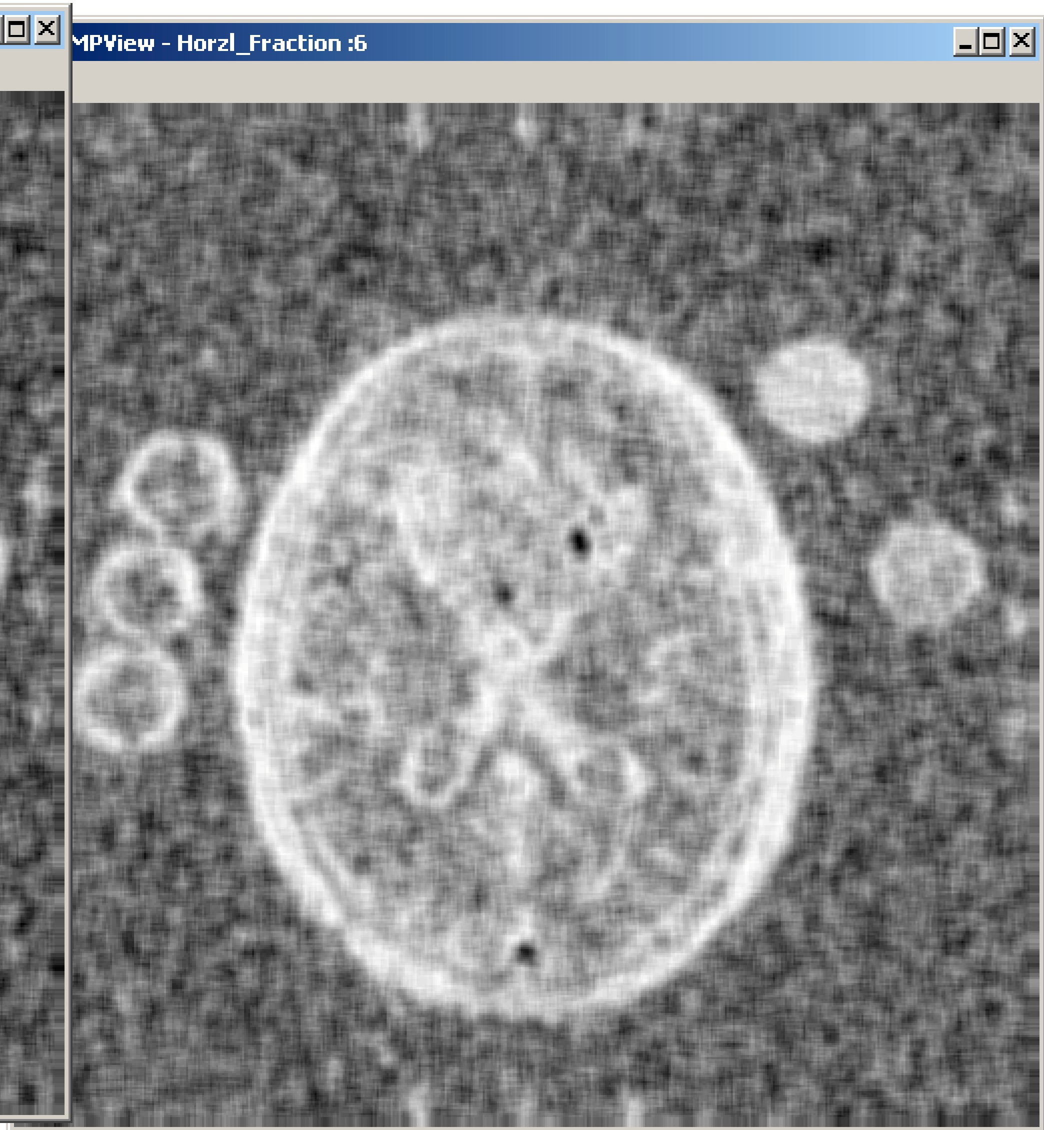
Texture feature maps

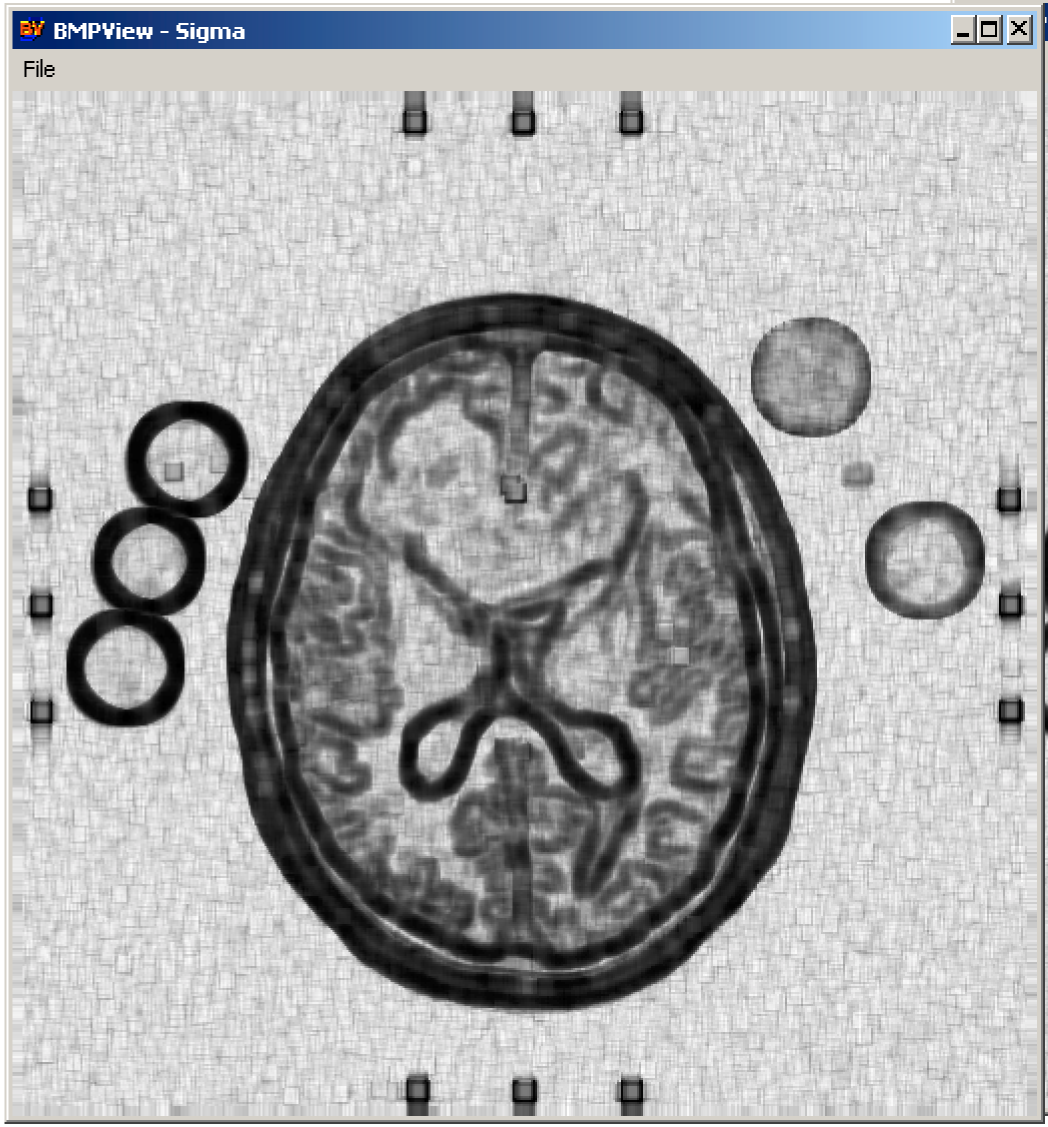
T1-weighted pre Gd 763-2-30

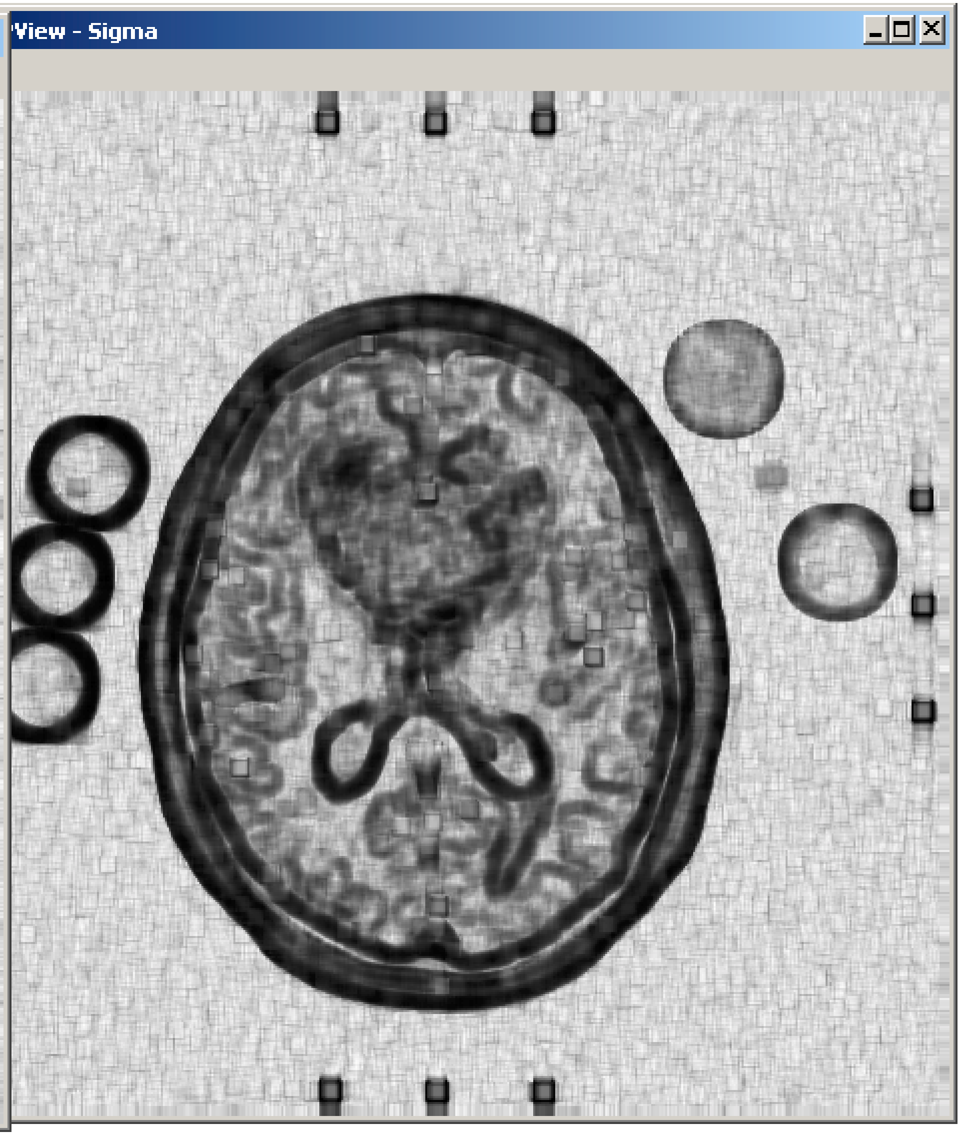


T1-weighted post Gd 763-4-176



Arvid Lundervold
COST B11 WG 3
Angers, 2001





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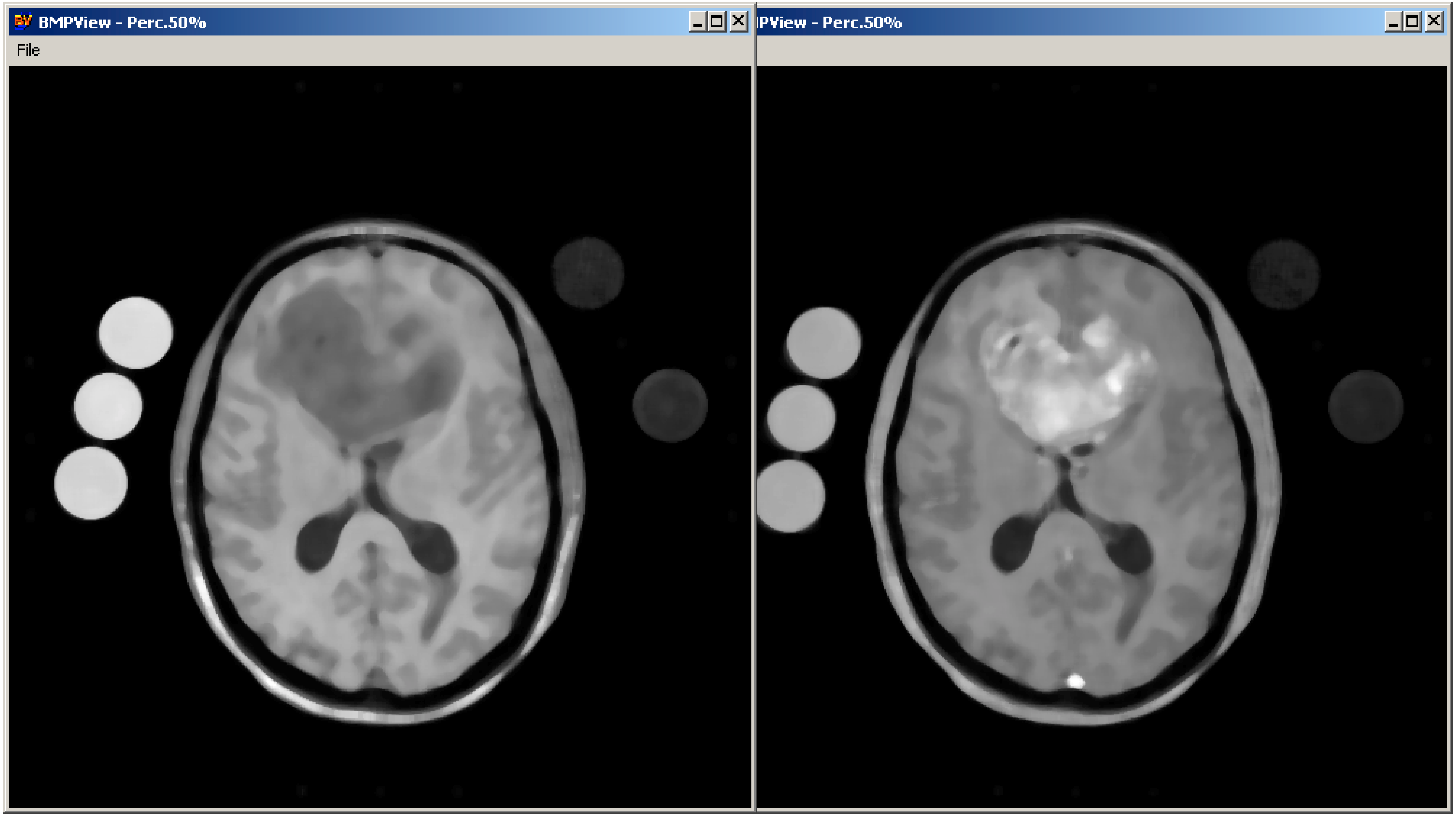

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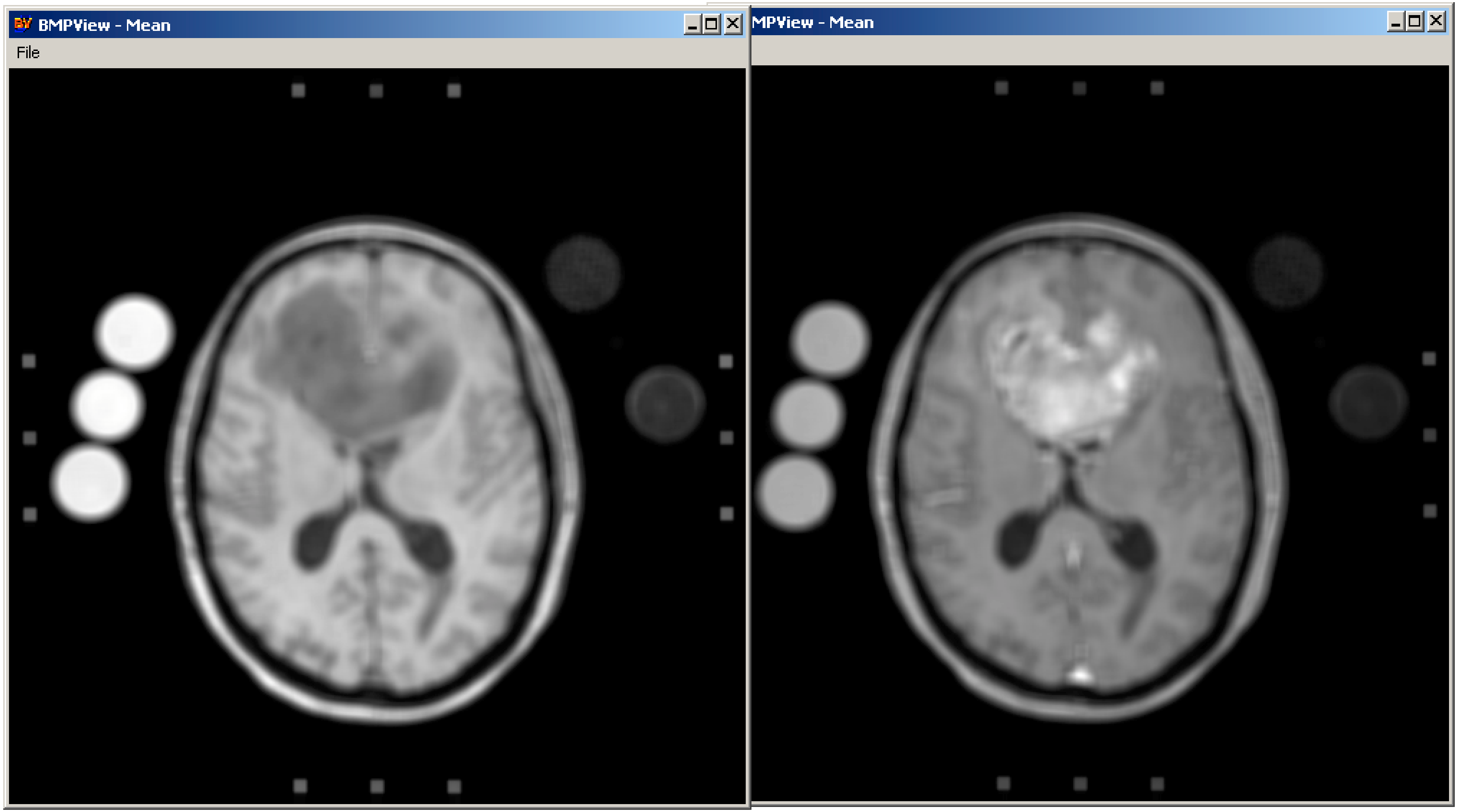
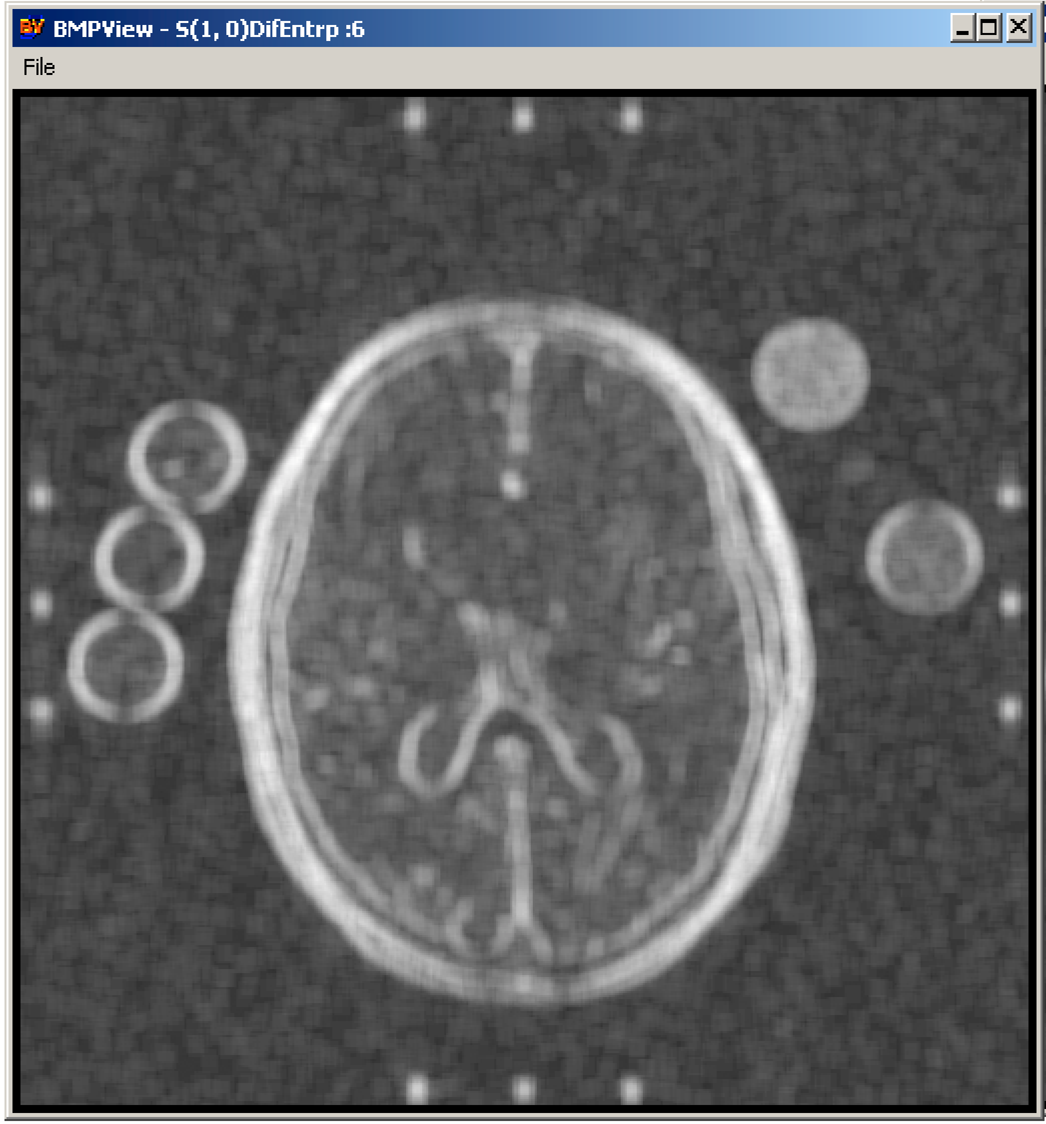
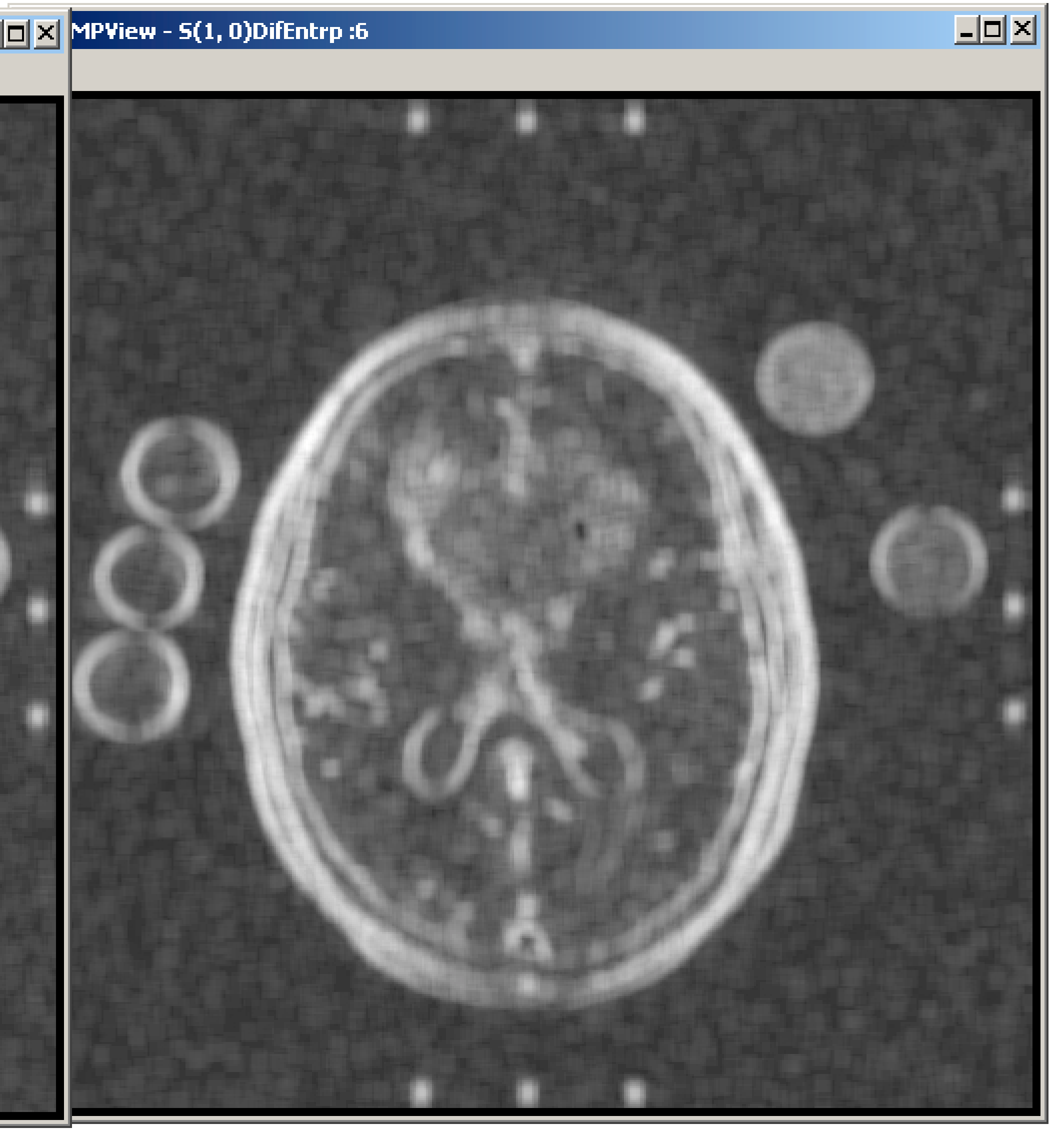
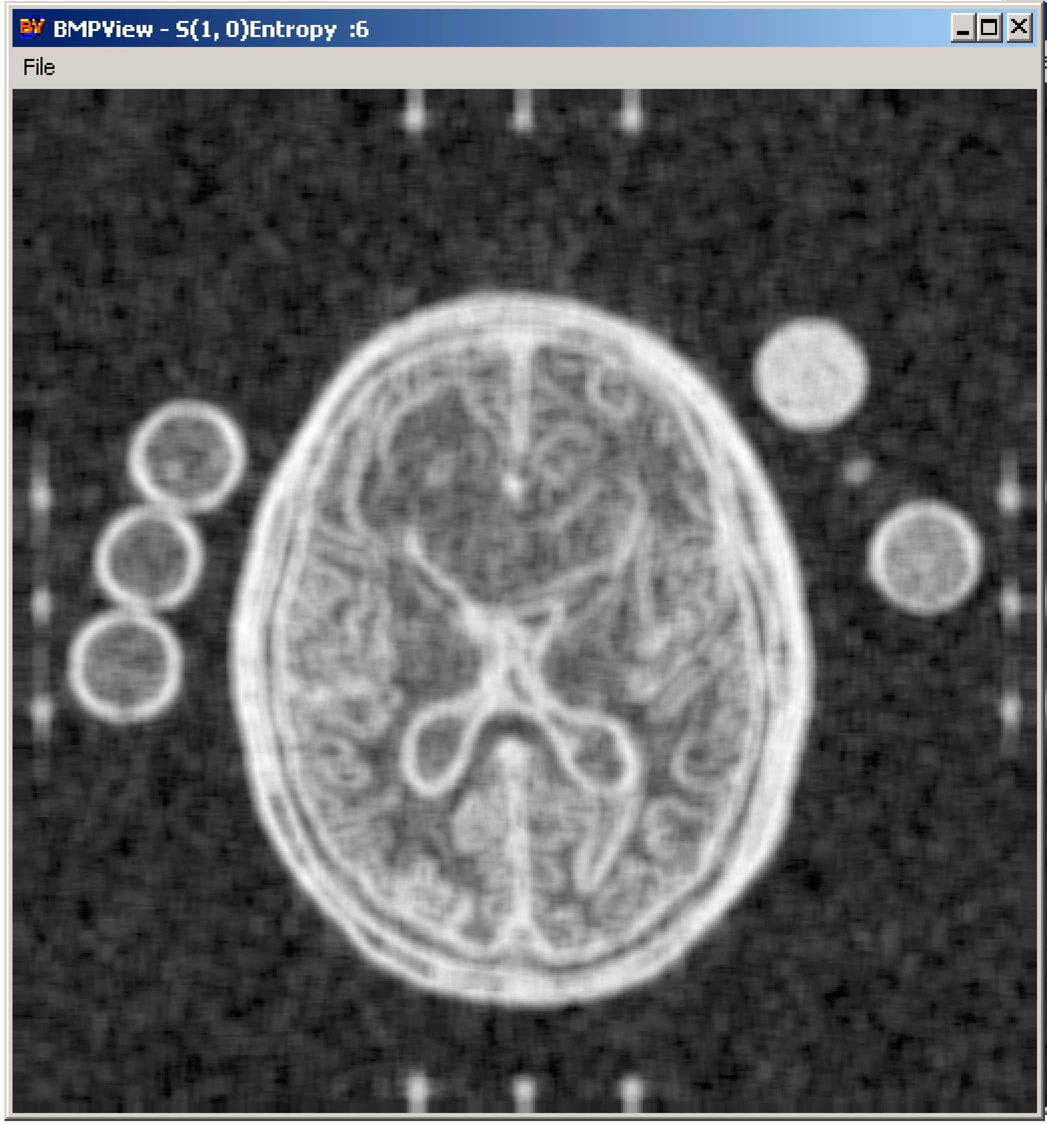
COST B11 WG 3
Angers, 2001

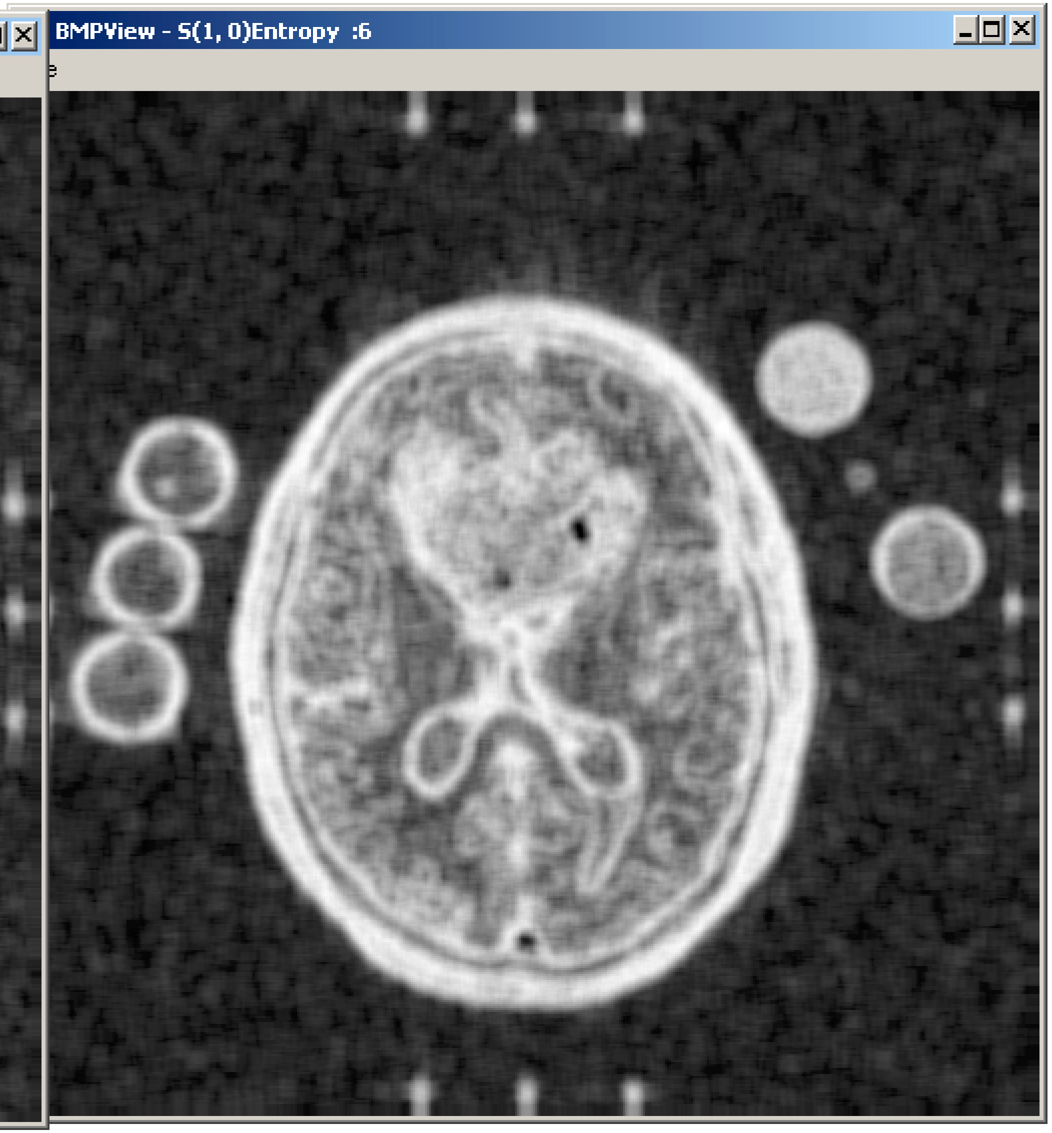


Arvid Lundervold
COST B11 WG 3
Angers, 2001


BMPView - S(1, 0)DifEntrp :6
File


MPView - S(1, 0)DifEntrp :6





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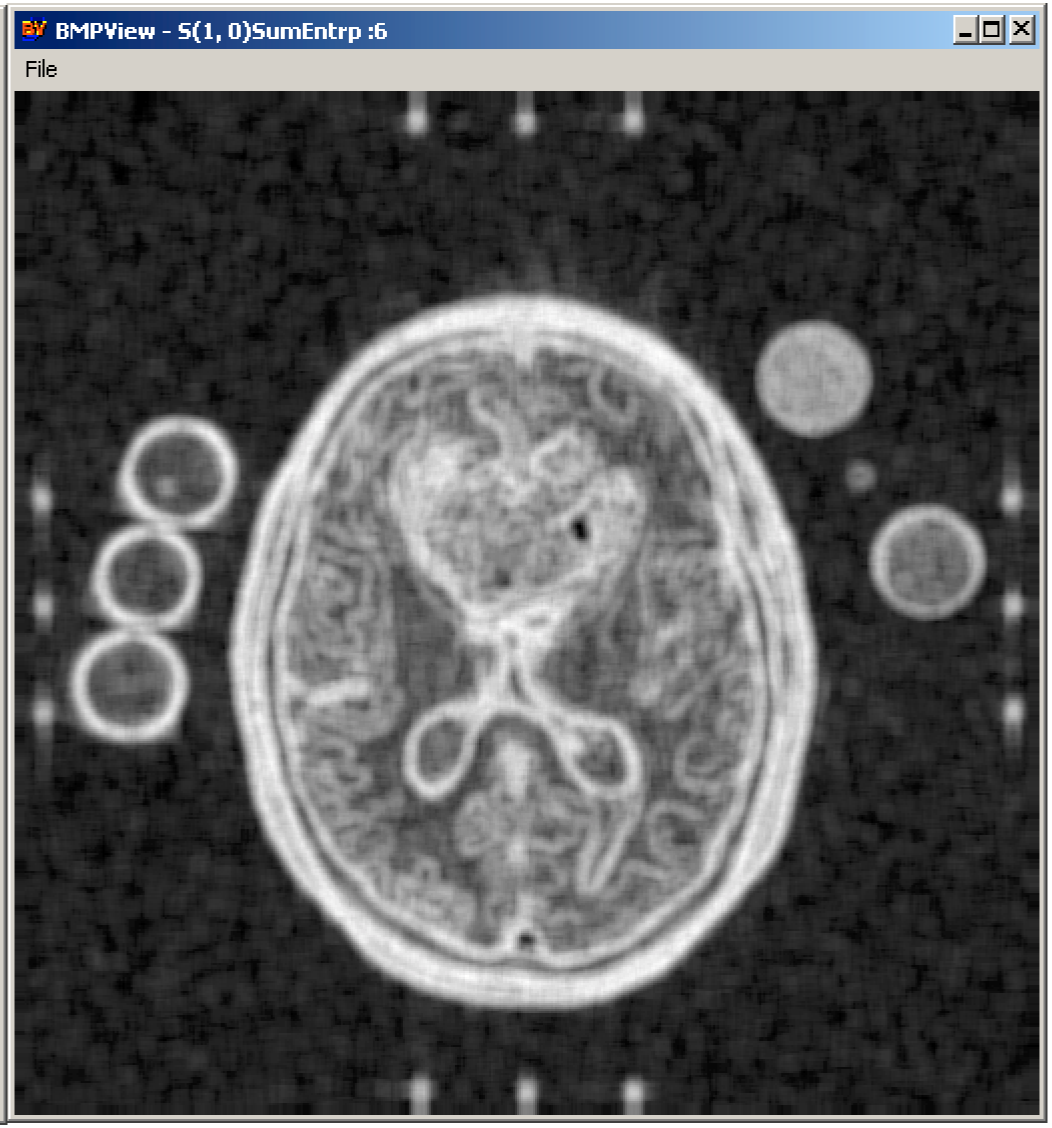
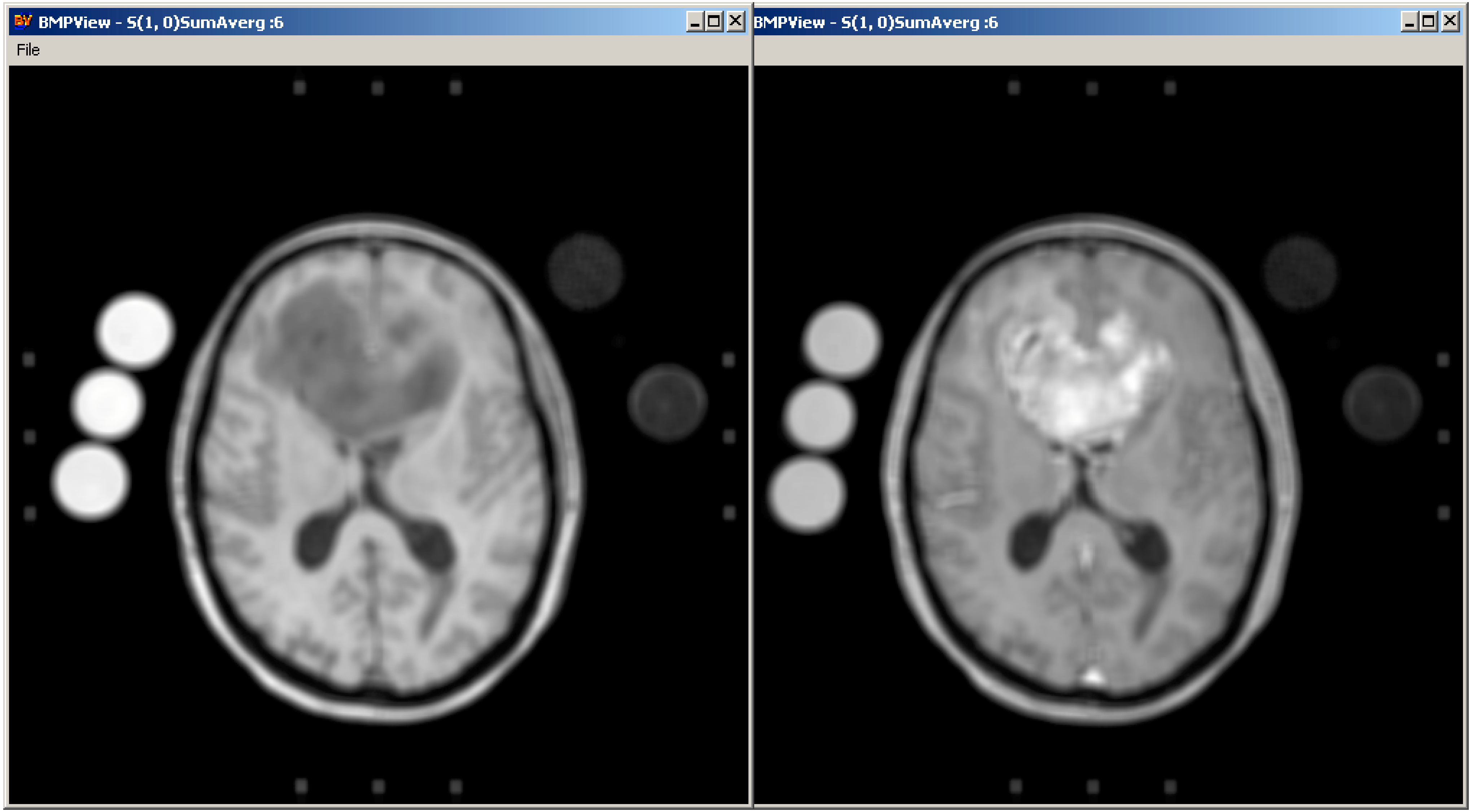
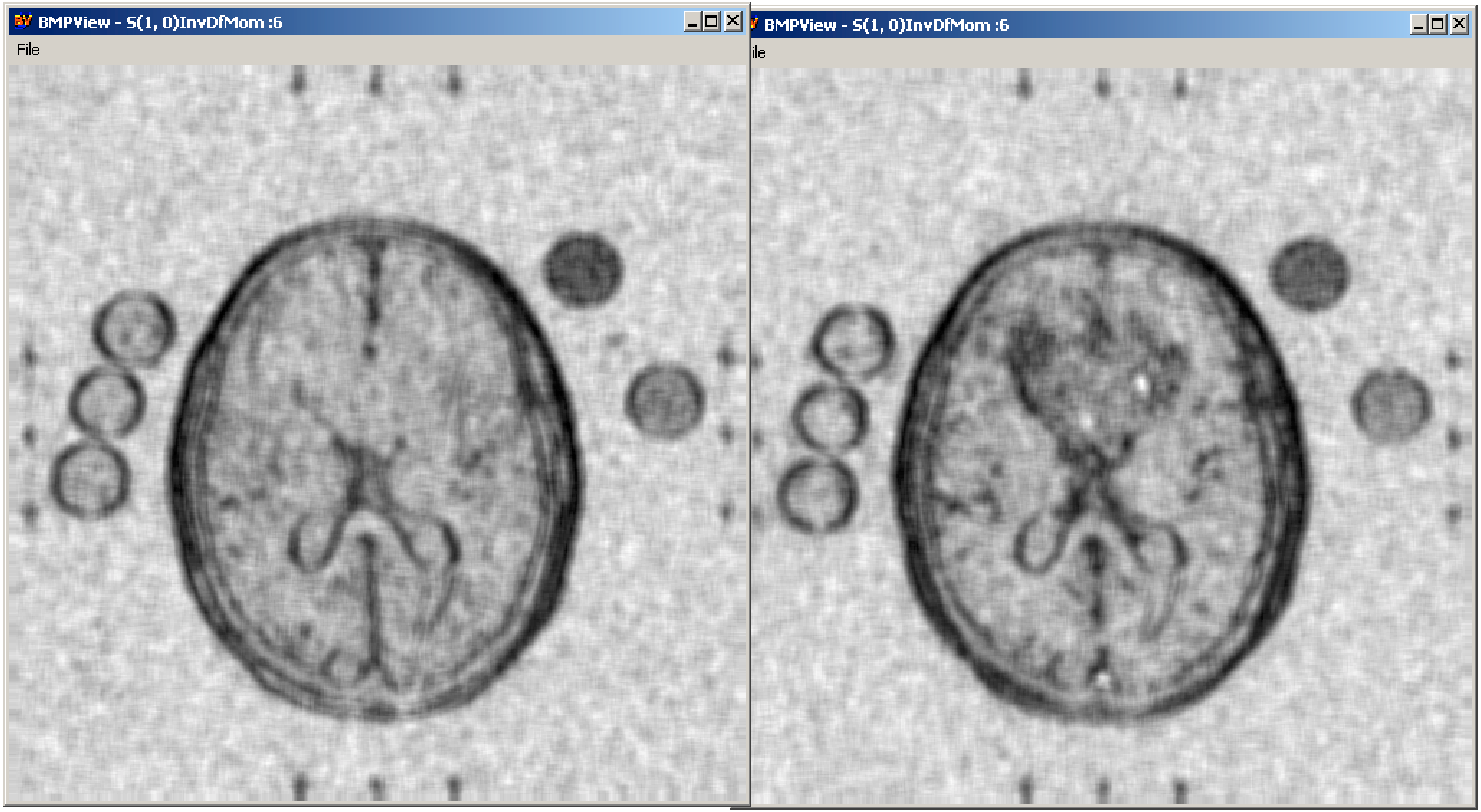
COST B11 WG 3
Angers, 2001



Arvid Lundervold
COST B11 WG 3
Angers, 2001



Arvid Lundervold
COST B11 WG 3
Angers, 2001



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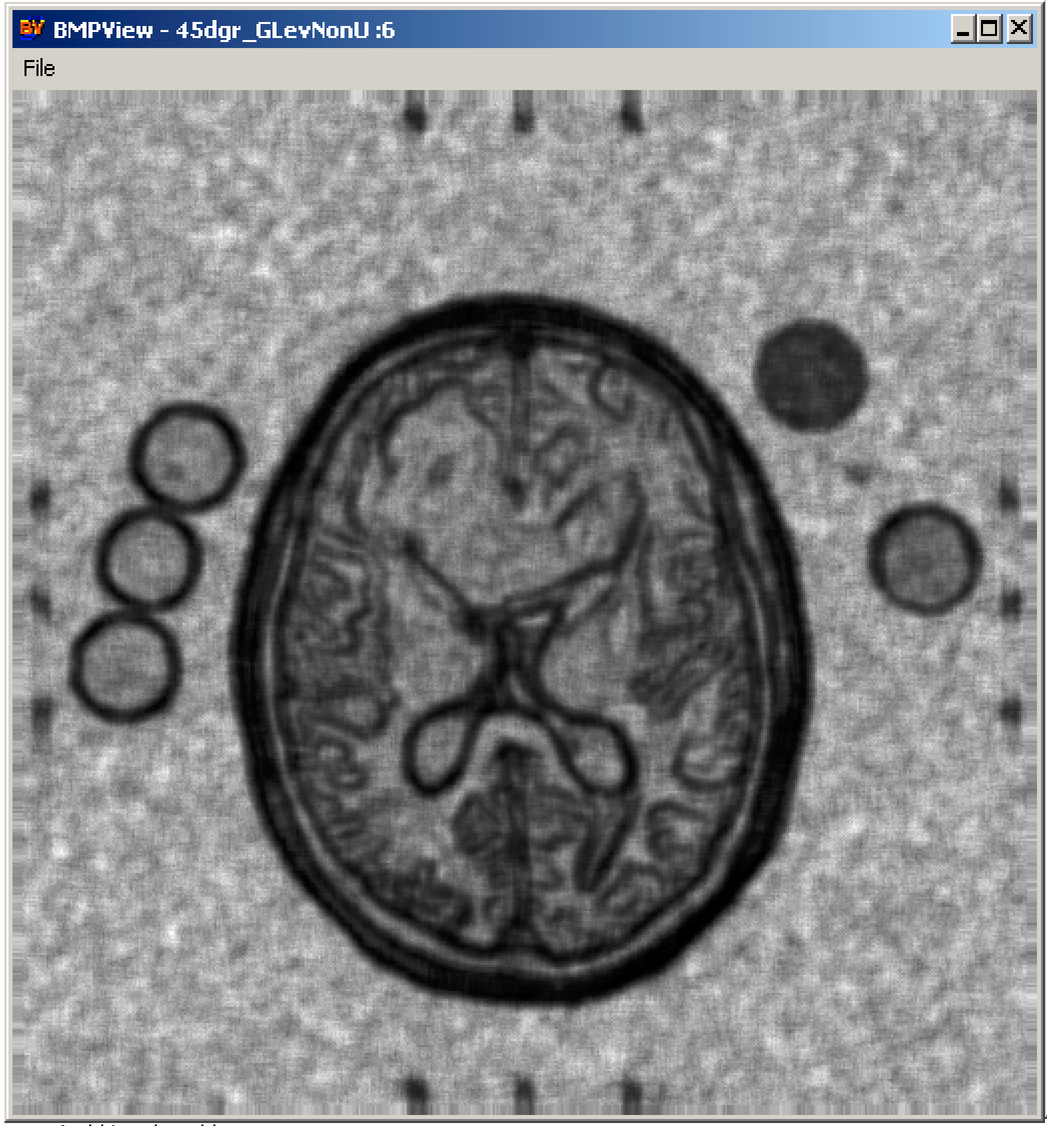
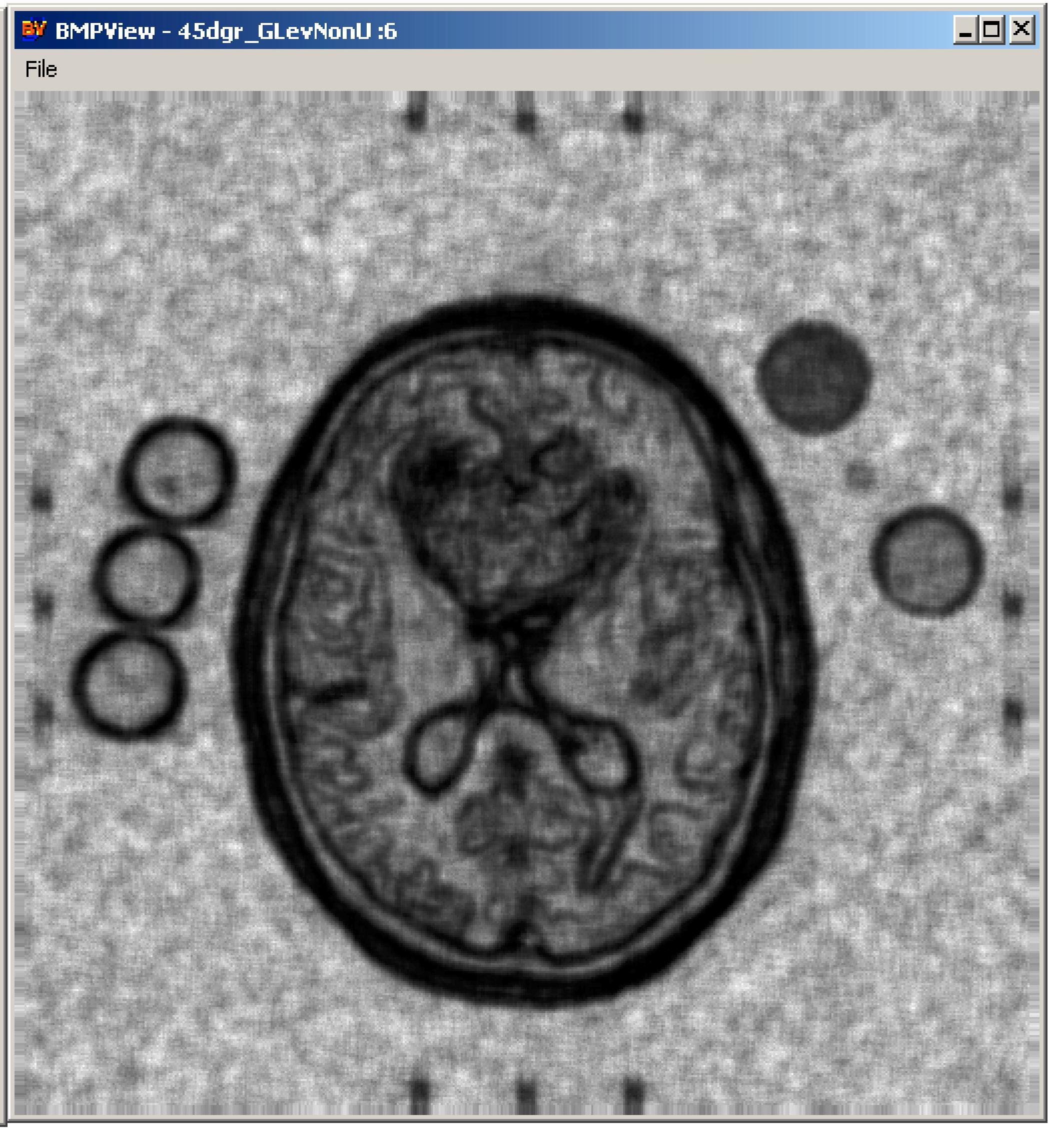
COST B11 WG 3
Angers, 2001





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COST B11 WG 3
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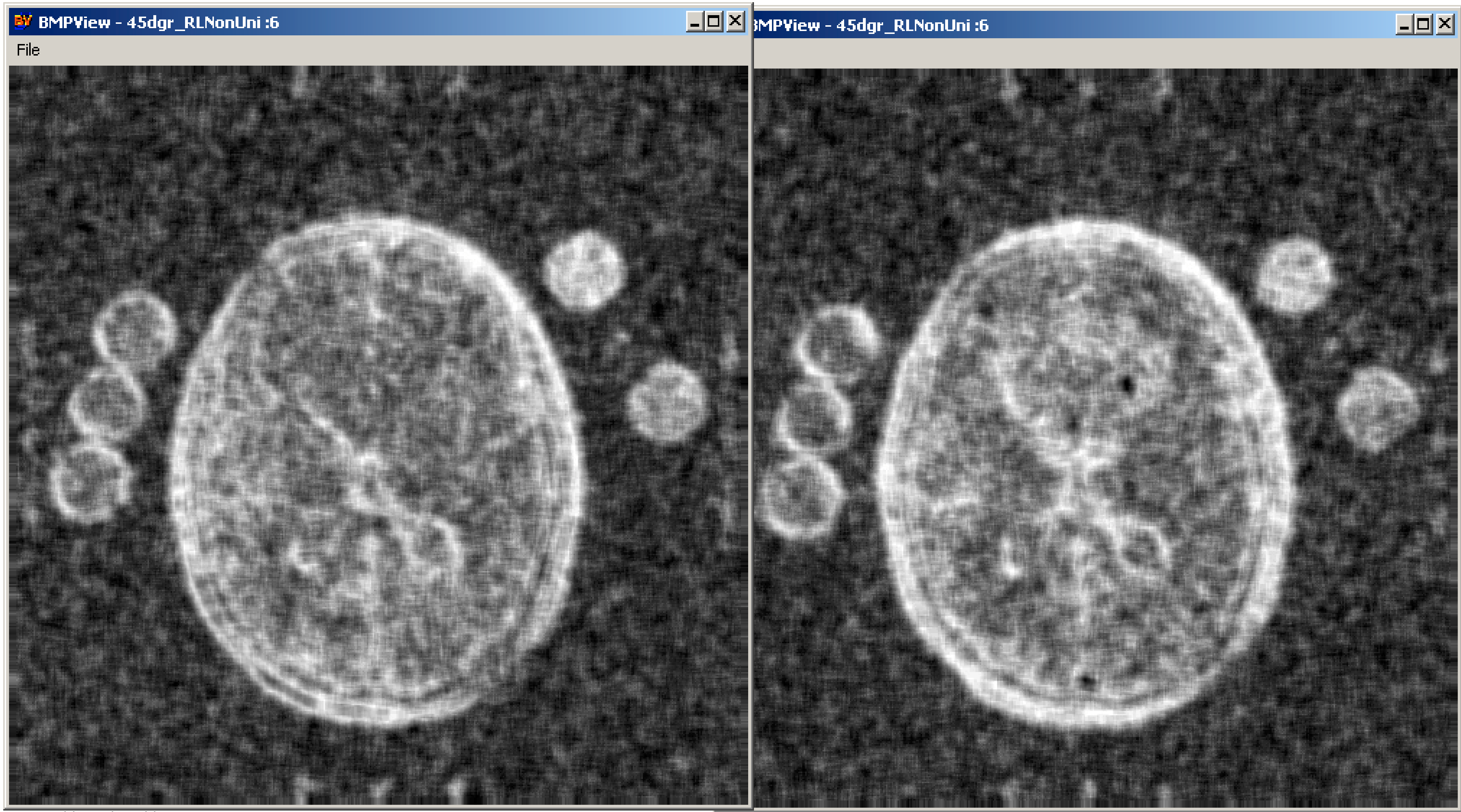

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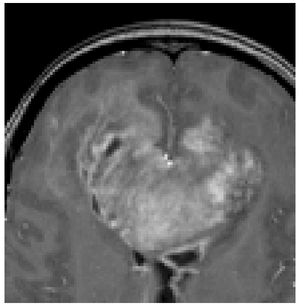
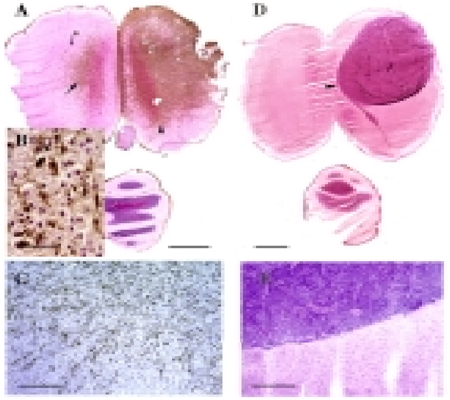
Some conclusions and perspectives ...

- Glioma is a good driving application to explore different structural and functional MR imaging techniques allowing histological verification of MR findings and postprocessing results



- In experimental brain tumors such verification can be done slice-by-slice, and different tissue tissue textures ca be “engineered” by using different tumor cell-lines.



- The value of texture analysis in MRI can be improved when texture features are extended to 3D imaging (“3D texture”) and multispectral imaging (“color texture”).

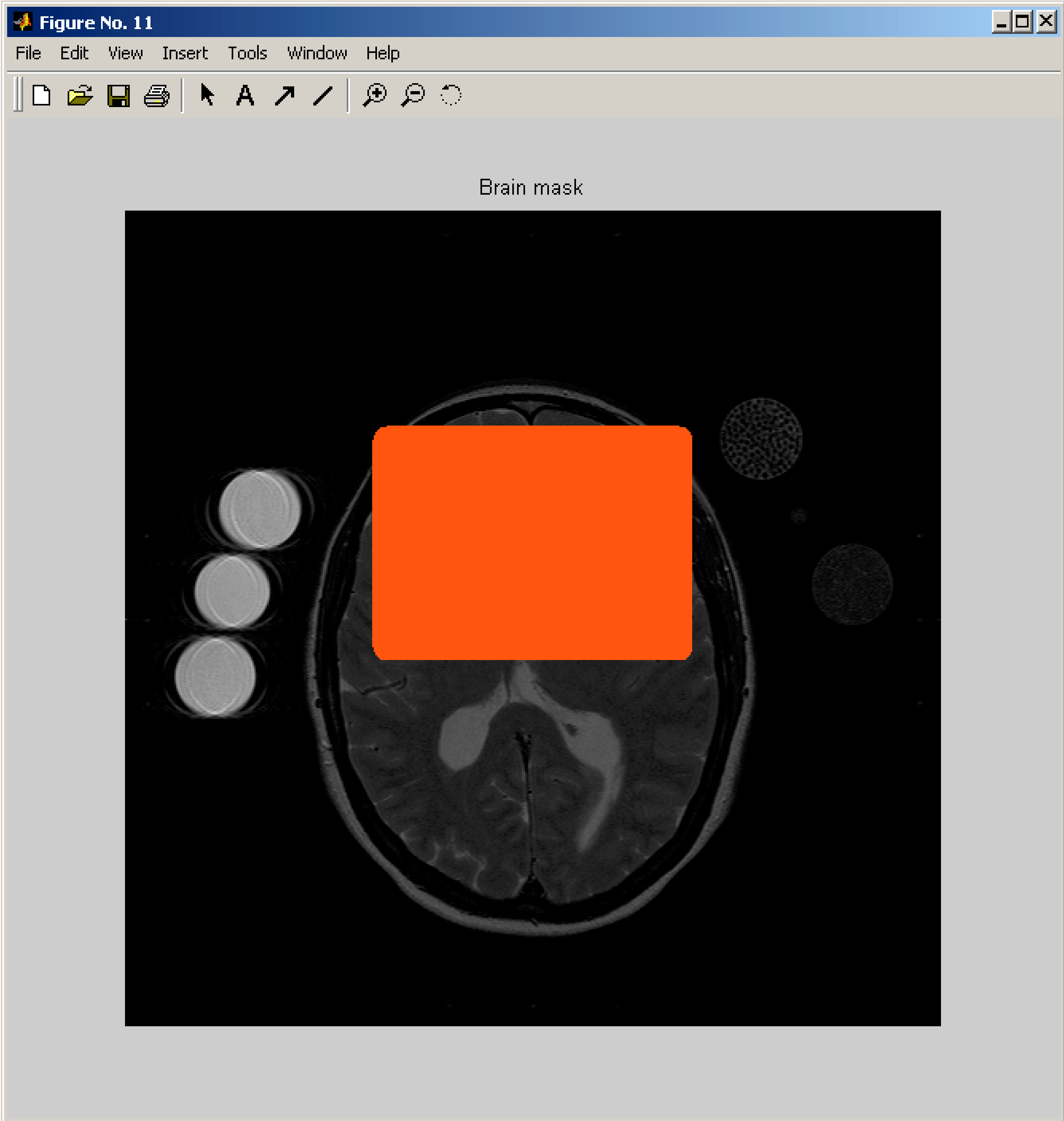
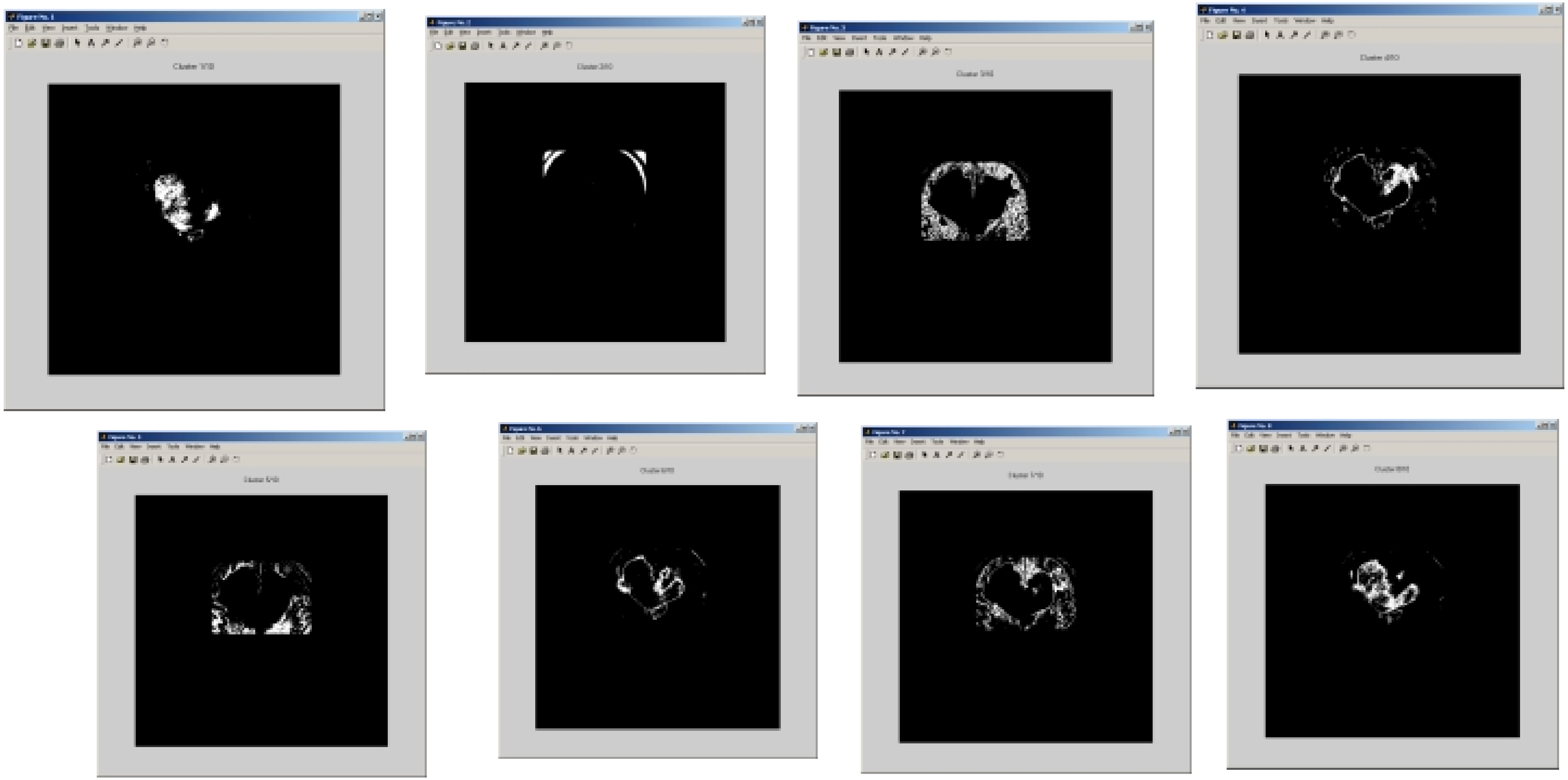
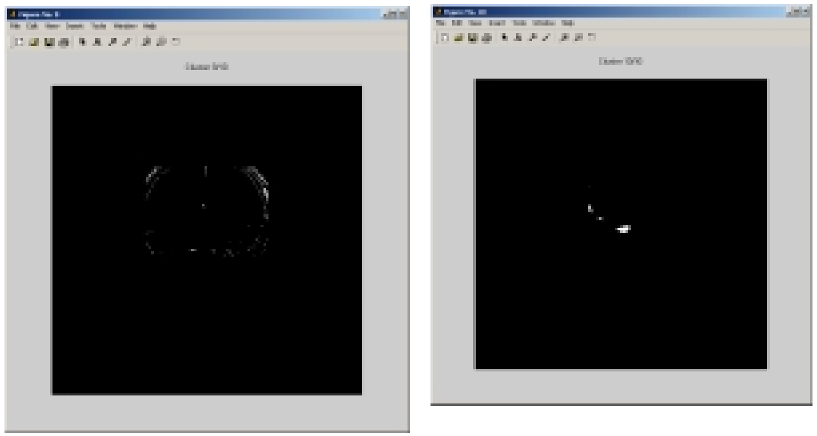


Figure No. 11
File Edit View Insert Tools Window Help
Brain mask





k-means clustering

k=10

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Definitions of texture parameters computed by MaZda :

Histogram

Histogram-based features

Note

To keep consistency with the formulas used in the standard references [1], [2] on texture analysis, it is assumed in MaZda that the intensity of image under analysis changes from 1 to *Ng*, where $Ng = 2^k$, and *k* is the number of bits per pixel. Thus if originally the image intensity changes from 0 to *Ng*-1, MaZda converts this image internally, such that its intensity changes from 1 to *Ng*. Consequently, the summation indices in the formulas listed below span the range from 1 to *Ng*.

In the formulas that follow, $p(i)$ is a normalized histogram vector (i.e. histogram whose entries are divided by the total number of pixels in ROI), i=1,2,..., N_g, and N_g denotes the number of intensity levels.

Mean: $$\mu = \sum_{i=1}^{N_g} i p(i)$$

Variance: $$\sigma^2 = \sum_{i=1}^{N_g} (i-\mu)^2 p(i)$$

Skewness: $$\mu_3 = \sigma^{-3} \sum_{i=1}^{N_g} (i-\mu)^3 p(i)$$

Kurtosis: $$\mu_4 = \sigma^{-4} \sum_{i=1}^{N_g} (i-\mu)^4 p(i) - 3$$

References

[1] R. Haralick, K. Shanmugam and I. Dinstein, Textural Features for Image Classification, *IEEE Transactions on Systems, Man and Cybernetics*, **3**, 6, 1973, 610-621.

[2] R. Haralick, Statistical and Structural Approaches to Texture, *Proceedings IEEE*, **67**, 5, 1979, 786-804.

[3] R. Lerski, K. Straughan, L. Shad, D. Boyce, S. Bluml and I. Zuna, MR Image Texture Analysis – An Approach to Tissue Characterization, *Magnetic Resonance Imaging*, **11**, 1993, 873-887.

[4] A. Materka and M. Strzelecki, *Texture Analysis Methods – A Review*, COST B11 report (presented and distributed at MC meeting and workshop in Brussels, June 1998), Technical University of Lodz, Poland, 1998.

[5] Y. Hu and T. Dennis, Textured Image Segmentation by Context Enhanced Clustering, *IEE Proc.-Visual Image and Signal Processing*, **141**, 6, 1994, 413-421.

Gradient

For the gradient feature calculation the following neighborhood for image pixel $x(i,j)$ is defined:

A	B	C	D	E
F	G	H	I	J
K	L	$x(i,j)$	N	O
P	Q	R	S	T
U	V	W	Y	Z

Based on this neighborhood, the absolute gradient value ($ABSV(i,j)$) is calculated for each pixel:

a) for 5x5 pixel neighborhood: $ABSV5(i,j) = \sqrt{(W-C)^2 + (O-K)^2}$

b) for 3x3 pixel neighborhood: $ABSV3(i,j) = \sqrt{(R-H)^2 + (N-L)^2}$

The $ABSV3$ definition is used in MaZda version 2.13. For the $ABSV$=$ABSV3$ matrix of M elements (which contains absolute gradient values for ROI pixels), the gradient features are defined as follows:

Gradient-based parameters

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Mean absolute gradient: $\mathrm{GrMean} = \frac{1}{M} \sum_{i,j \in ROI} ABSV(i,j)$

Variance of absolute gradient: $\mathrm{GrVariance} = \frac{1}{M} \sum_{i,j \in ROI} (ABSV(i,j) - \mathrm{GrMean})^2$

Skewness of absolute gradient:

$$\mathrm{GrSkewness} = \frac{1}{(\sqrt{\mathrm{GrVariance}})^3} \frac{1}{M} \sum_{i,j \in ROI} (ABSV(i,j) - \mathrm{GrMean})^3$$

Kurtosis of absolute gradient:

$$\mathrm{GrKurtosis} = \frac{1}{(\sqrt{\mathrm{GrVariance}})^4} \frac{1}{M} \sum_{i,j \in ROI} (ABSV(i,j) - \mathrm{GrMean})^4 - 3$$

where ROI is a region of interest.

Percentage of non-zero $ABSV$ matrix elements (**Grads>0**)

RLM

Run length matrix-based parameters

Let $p(i,j)$ be the number of times there is a run of length j having grey level i. Let N_g be the number of grey levels and N_r be the number of runs. Definitions of the parameters of the run-length matrix $p(i,j)$, as adopted in MaZda, are given below.

Short run emphasis inverse moments:

$$\text{ShrtREmph} = \left(\sum_{i=1}^{N_g}\sum_{j=1}^{N_r}\frac{p(i,j)}{j^2}\right)/C$$

Long run emphasis moments:

$$\text{LngREmph} = \left(\sum_{i=1}^{N_g}\sum_{j=1}^{N_r} j^2 p(i,j)\right)/C$$

Grey level nonuniformity:

$$\text{GLevNonUni} = \left(\sum_{i=1}^{N_g}\left(\sum_{j=1}^{N_r} p(i,j)\right)^2\right)/C$$

Run length nonuniformity:

$$\text{RLNonUni} = \left(\sum_{j=1}^{N_r}\left(\sum_{i=1}^{N_g} p(i,j)\right)^2\right)/C$$

Fraction of image in runs:

$$\text{Fraction} = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} p(i,j) \Big/ \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} j\,p(i,j)$$

The coefficient C is defined as

$$C = \sum_{i=1}^{N_g}\sum_{j=1}^{N_r} p(i,j)$$

The above five features are calculated for four directions: horizontal (Horzl_), vertical (Vertl_), slanted at 45 degrees (45dgr_) and slanted at 135 degrees (135dgr_). The RL feature name in MaZda software contains a prefix that defines direction and feature type, for example 45dgr_RLNonUni means the run length nonuniformity calculated for 45-degree direction.

The second-order histogram is defined as the co-occurrence matrix $h_{d\theta}(i,j)$ [1]. When divided by the total number of neighboring pixels $R(d, \theta)$ in ROI, this matrix becomes the estimate of the joint probability, $p_{d\theta}(i,j)$, of two pixels, a distance d apart along a given direction θ having particular (co-occurring) values i and j. Formally, given the image $f(x,y)$ with a set of N_g discrete intensity levels, the matrix $h_{d\theta}(i,j)$ is defined such that its (i,j)th entry is equal to the number of times that

$f(x_1,y_1)=i$ and $f(x_2,y_2)=j$,

where $(x_2,y_2)=(x_1,y_1)+(d\cos\theta, d\sin\theta)$.

This yields a square matrix of dimension equal to the number of intensity levels in the image, for each distance d and orientation θ. In MaZda, the distances d = 1, 2, 3, 4 and 5 pixels with angles θ = 0°, 45°, 90° and 135° are considered. Reduction of the number of intensity levels (by quantization to fewer levels of intensity) helps increase the speed of computation, with some loss of textural information.

The co-occurrence matrix-derived parameters computed by MaZda are defined by the equations that follow, where μ_x, μ_y and σ_x, σ_y denote the mean and standard deviations of the row and column sums of the co-occurrence matrix, respectively [related to the marginal distributions $p_x(i)$ and $p_y(j)$]. R is the total number of neighboring pixel pairs, which normalizes the co-occurrence matrix to the probability distribution.

COM

Entropy:

$$\text{Entropy} = -\frac{1}{R}\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)\log\left(\frac{1}{R}p(i,j)\right)$$

Difference variance:

$$\text{DifVarnc} = \sum_{i=0}^{N_g-1}(i-\mu_{x-y})^2 p_{x-y}(i)$$

where μ_{x-y} is a mean value of difference distribution p_{x-y}:

$$p_{x-y}(k) = \frac{1}{R}\sum_{\substack{i=1 \\ |i-j|=k}}^{N_g}\sum_{j=1}^{N_g} p(i,j) \qquad k = 0,1,\ldots,N_g-1$$

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Co-occurrence matrix-derived parameters

Angular second moment:

$$\text{AngScMom} = \frac{1}{R^2}\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} p(i,j)^2$$

Contrast:

$$\text{Contrast} = \frac{1}{R}\sum_{n=0}^{N_g-1} n^2 \sum_{\substack{i=1 \\ |i-j|=n}}^{N_g}\sum_{j=1}^{N_g} p(i,j)$$

Correlation:

$$\text{Correlat} = \frac{\frac{1}{R}\sum_{i=1}^{N_g}\sum_{j=1}^{N_g} ij\,p(i,j) - \mu_x\mu_y}{\sigma_x\sigma_y}$$

Sum of squares:

$$\text{SumOfSqs} = \frac{1}{R}\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}(i-\mu_x)^2 p(i,j)$$

Inverse difference moment:

$$\text{InvDfMom} = \frac{1}{R}\sum_{i=1}^{N_g}\sum_{j=1}^{N_g}\frac{1}{1+(i-j)^2}p(i,j)$$

Sum average:

$$\text{SumAverg} = \sum_{i=1}^{2N_g} i\,p_{x+y}(i)$$

where

$$p_{x+y}(k) = \frac{1}{A}\sum_{\substack{i=1 \\ i+j=k}}^{N_g}\sum_{j=1}^{N_g} p(i,j) \qquad k = 2,3\ldots,2N_g$$

Sum variance:

$$\text{SumVarnc} = \sum_{i=1}^{2N_g}(i-x_8)^2 p_{x+y}(i)$$

Sum entropy:

$$\text{SumEntrp} = -\sum_{i=1}^{2N_g} p_{x+y}(i)\log(p_{x+y}(i))$$

Difference entropy:

$$\text{DifEntrp} = -\sum_{i=1}^{N_g} p_{x-y}(i)\log(p_{x-y}(i))$$

AR

Autoregressive model parameters

The autoregressive (AR) model assumes a local interaction between image pixels in that pixel intensity is a weighted sum of neighbouring pixel intensities. Assuming image f is a zero-mean random field, an AR causal model can be defined as

$$f_s = \sum_{r \in N_s} \theta_r f_r + e_s$$

where f_s is image intensity at site s, e_s denotes an independent and identically distributed (i.i.d.) noise, N_s is a neighbourhood of s, and $\boldsymbol{\theta}$ is a vector of model parameters. The local neighbourhood for AR model implemented in MaZda, represented by 4 parameters, is shown in Fig. 7.1. Shaded area in Fig. 7.1 indicates region where valid causal half-plane AR model neighbourhood may be located, in general.

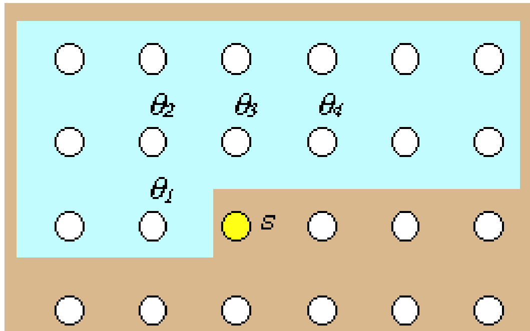

Fig. 7.1. Local neighbourhood of image element f_s

Using the AR model for image segmentation consists in identifying the model parameters for a given image region and then using the obtained parameter values for texture discrimination. In the case of simple pixel neighbourhood shown in Fig. 7.1, that comprises 4 immediate pixel neighbours, there are 5 unknown model parameters – the standard deviation σ of the driving noise e_s and the model parameter vector $\boldsymbol{\theta}=[\theta_1,\theta_2,\theta_3,\theta_4]$. The parameters can be estimated by minimizing the sum of squared error

$$\sum_s e_s^2 = \sum_s \left(f_s - \hat{\boldsymbol{\theta}} \boldsymbol{w}_s\right)^2$$

which leads to the following linear equations:

$$\hat{\boldsymbol{\theta}} = \left(\sum_s \boldsymbol{w}_s \boldsymbol{w}_s^T\right)^{-1} \left(\sum_s \boldsymbol{w}_s f_s\right)$$

$$\hat{\sigma}^2 = N^{-2} \sum_s \left(f_s - \hat{\boldsymbol{\theta}} \boldsymbol{w}_s\right)^2$$

where $\boldsymbol{w}_s = \mathrm{col}[f_i, i \in \mathrm{N}_s]$, and the square $N \times N$ image is assumed. The above set of equations is numerically solved in MaZda for each ROI of interest.

Image conversion in Matlab

```
function A = al_dcm2raw(file_dir, filename, xsize, ysize, d)
% AL_DCM2RAW read UINT16 binary xsize*ysize data with DICOM header, write as RAW
%  i.e.  <filename>.dcm --> <filename>.raw  in order to use .dcm-files
%  with Matlab and as 'raw' format in the MaZda MRI texture analysis software  (COST B11)
%  Arvid Lundervold, 10-APR-2001

[fname_dcm, errmsg] = sprintf('%s/%s.dcm', file_dir, filename);
[fname_raw, errmsg] = sprintf('%s/%s.raw', file_dir, filename);
[fid, message] = fopen(fname_dcm,'r','native');  % local MACHINEFORMAT

status = fseek(fid, -xsize*ysize*2, 'eof');  position = ftell(fid);  status = fseek(fid, position, 'bof');
[M, count] = fread(fid,[xsize,ysize],'uint16');
fclose(fid);
A = M';    %  A can now be displayed ………………..

% Write <filename>.raw image to disk
A_us = uint16(round(fliplr(A')));
[fid_raw, message] = fopen(fname_raw,'wb','n');
fwrite(fid_raw, A_us,'uint16');
fclose(fid_raw);
```

```
if d == 1    % Display image matrix A
  hi = max(max(A));
  lo = min(min(A));
  imagesc(A, [lo hi]); colormap(gray); colorbar('h'); axis image;
  [txt, errmsg] = sprintf('%s: min=%s max=%s',...
                    filename, num2str(lo), num2str(hi));
  title(txt);
end
```