Breast Cancer Analysis in DCE-MRI

Gabriele Piantadosi (PhD Candidate)

XXIX Cycle - III year presentation

Supervisor: Prof. Carlo Sansone
Co-Supervisor: Prof. Mario Sansone

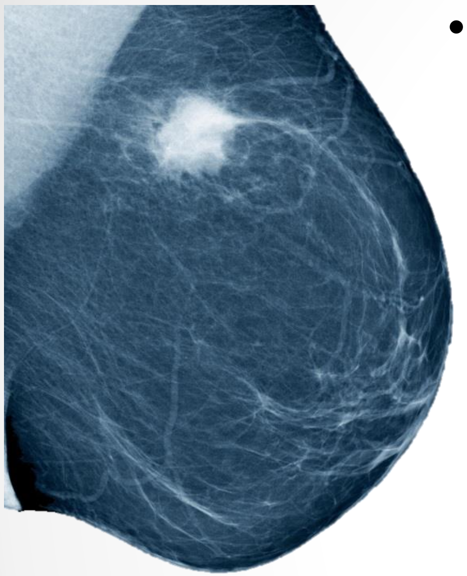
PhD candidate

- **Graduation:** MSc in Computer Engineering
- **Group:** PRIAMUS
- **Fellowship:** MIUR research grant
- **Research Field:** Breast Cancer Analysis in DCE-MRI
- **Study Activity:**

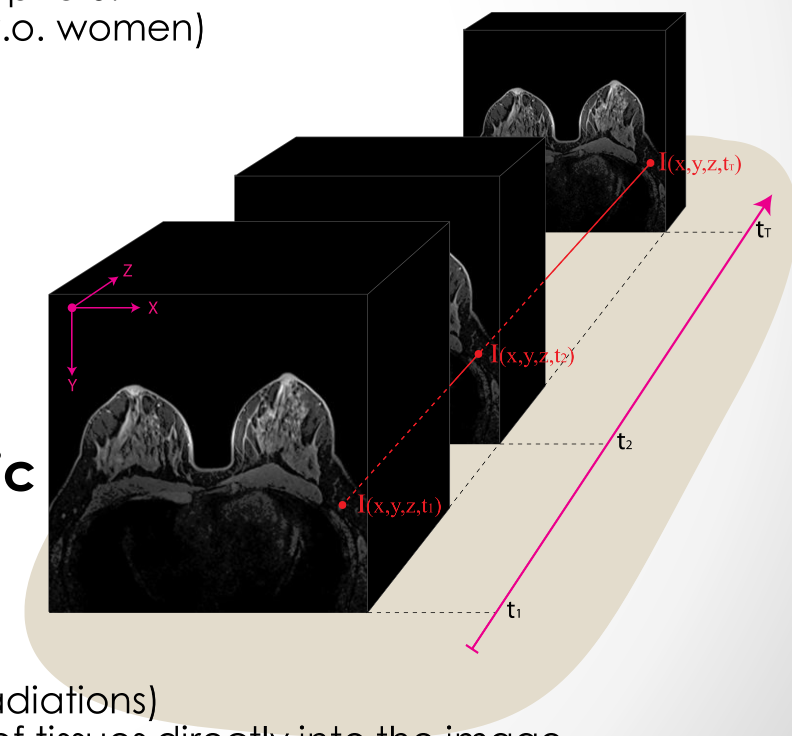
	Credits year 1								Credits year 2								Credits year 3									
	Estimated	bimonth 1	bimonth 2	bimonth 3	bimonth 4	bimonth 5	bimonth 6	Summary	Estimated	bimonth 1	bimonth 2	bimonth 3	bimonth 4	bimonth 5	bimonth 6	Summary	Estimated	bimonth 1	bimonth 2	bimonth 3	bimonth 4	bimonth 5	bimonth 6	Summary	Total	Check
Modules	26	0	3	0	3	3	11	20	15	3	7	0	3	0	6	19	5	0	0	0	0	0	0	0	39	30-70
Seminars	13	2.4	1	4.8	1	1.5	2.3	13	12	0.2	0.9	0	0	6.8	0	7.9	5	0	0	0	0	0	0.6	0.6	21.5	10-30
Research	21	7.6	6	5.2	6	5.5	0	30.3	33	6.8	2.1	10	7	3.2	4	33.1	50	10	10	10	10	10	9.4	59.4	122.8	80-140
	60	10	10	10	10	10	13.3	63.3	60	10	10	10	10	10	10	60	60	10	10	10	10	10	10	60	183.3	180

- **Activity abroad:** six months (from April to October 2016) at the University of South Florida (USF) under the supervision of the Prof. Lawrence O. Hall (Department of Computer Science and Engineering).
- **Thesis:** Pattern Recognition in Breast DCE-MRI Automatic Cancer Analysis

Mammography vs. MRI for Breast Cancer Analysis



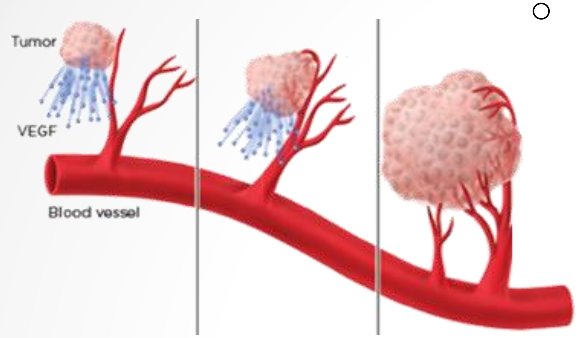
- **Mammography**
  - State of art of breast cancer screening
  - No contrast = Calcifications or masses must to be inspected via biopsy
  - Makes use of x-rays radiations (ionizing radiations)
  - Low 2D spatial resolution up to 0.2 mm^2
  - Not early detection (>40 y.o. women)
  - Low sensitivity (50% - 70%)



- **Dynamic Contrast Enhanced – Magnetic Resonance Imaging (DCE-MRI):**
  - High sensitivity (>95%)
  - Early detection (>20 y.o. women)
  - High 3D spatial resolution up to 0.01 mm^3
  - Makes use of electromagnetic fields (non-ionizing radiations)
  - The contrast agent provides functional information of tissues directly into the image

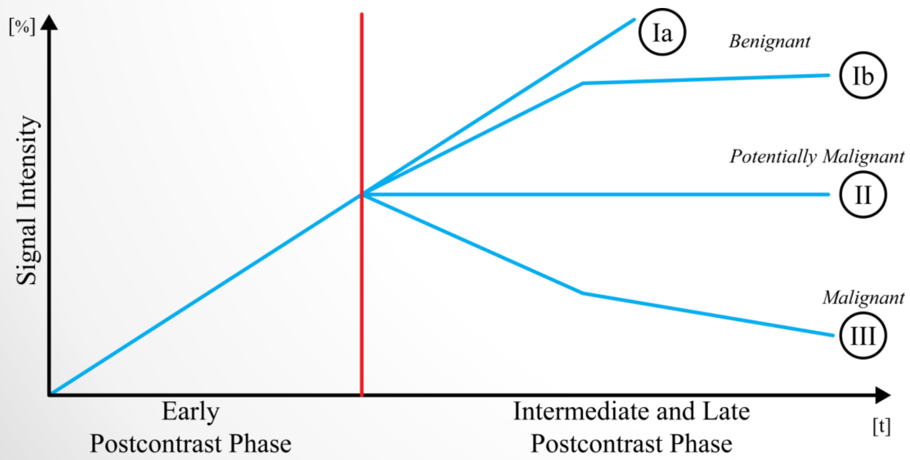
DCE-MRI in Breast Cancer Analysis

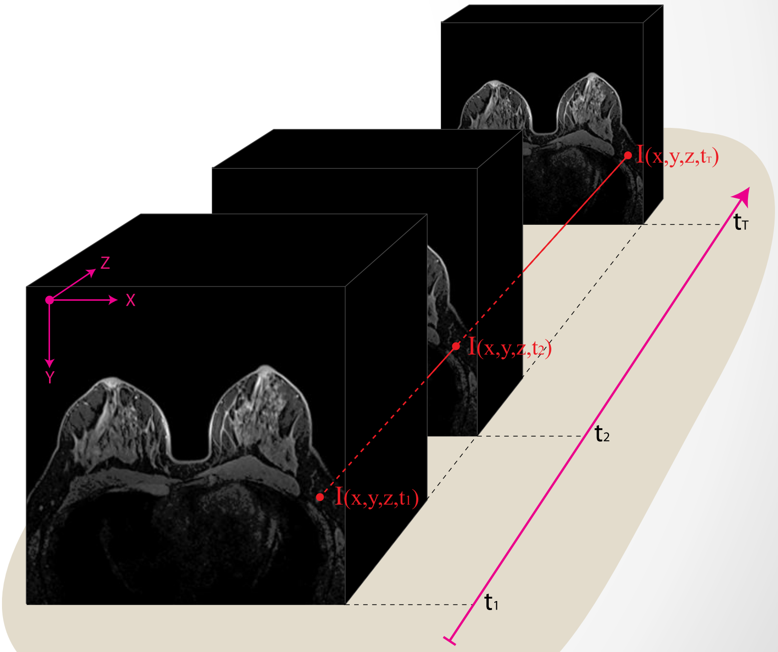
- **Dynamic contrast-enhanced MRI (DCE-MRI):**



  - By using a contrast agent (often gadolinium) provides a four dimensional volume
    - 3 Spatial (geometric information)
    - 1 Temporal (functional information) *(such as neo-angiogenesis)*

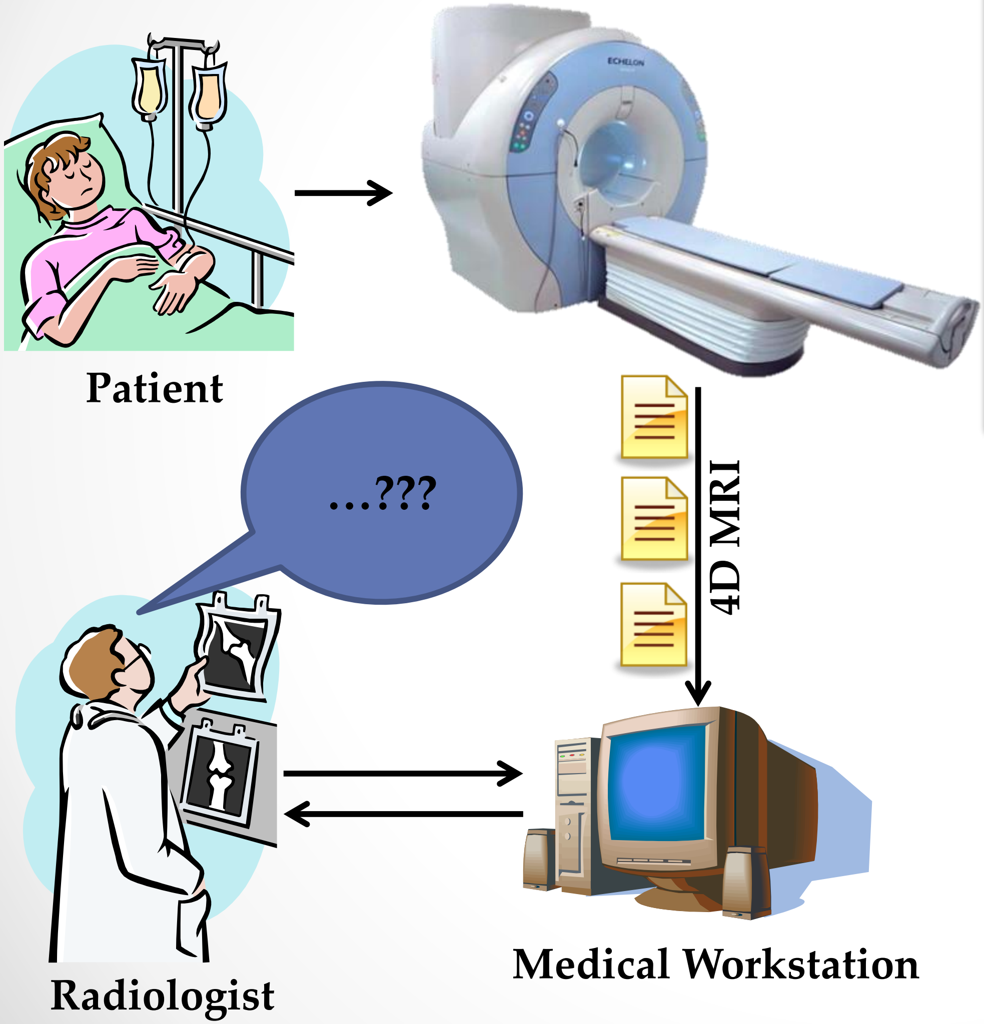
- **Time Intensity Curve (TIC)**
  - Shows the trend of the contrast agent absorption
  - "Visual" assessment of a DCE-MRI among TIC
  - Error prone → Computer-Aided





- **Type I:** Persistent (normal or benign lesion)
- **Type II:** Plateau (potentially malignant lesion)
- **Type III:** Washout (malignant lesion)

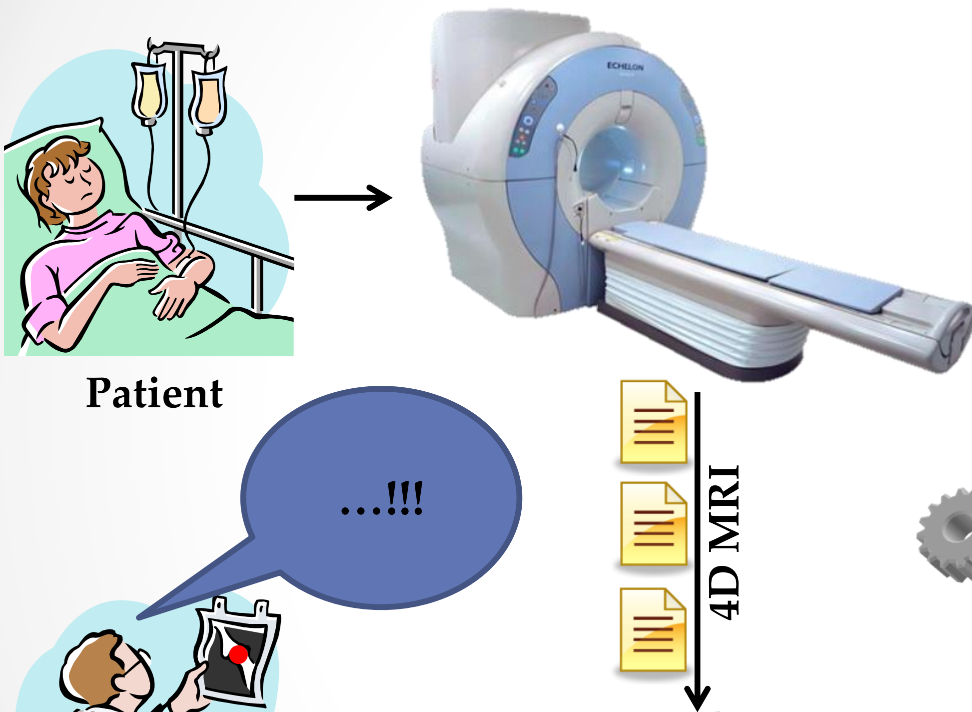
Clinical Scenario (1/2)

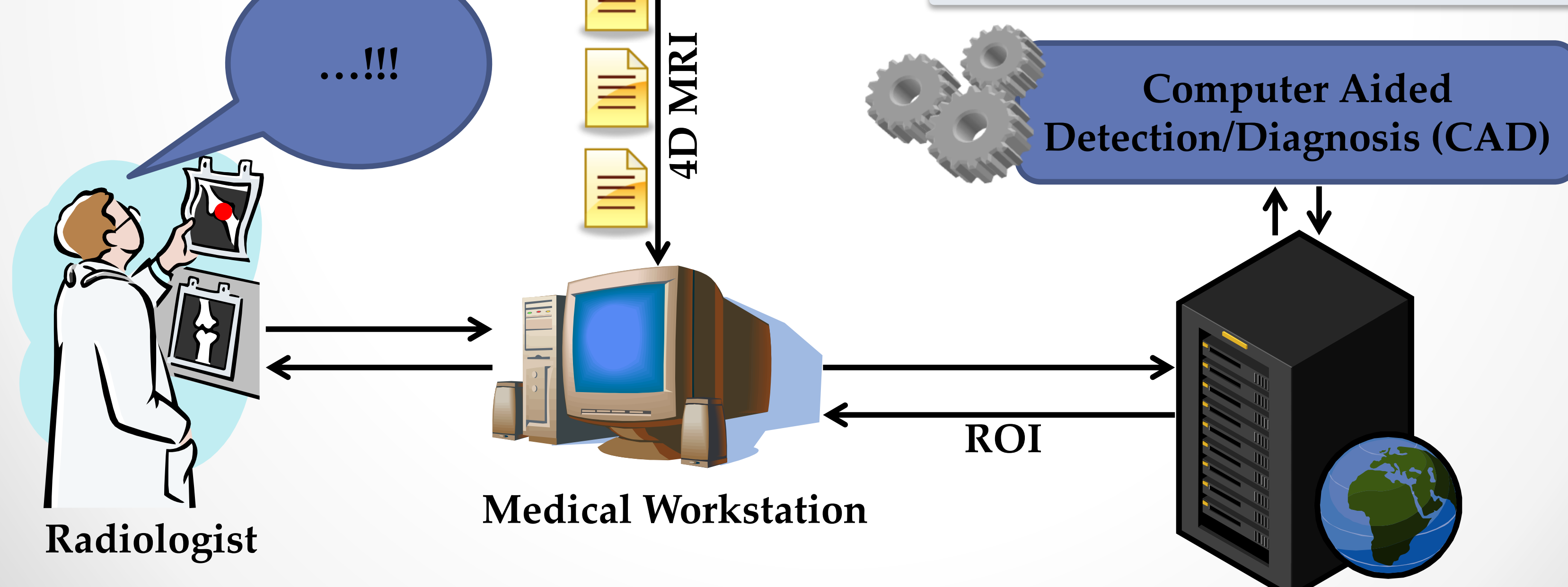


The Patient performs a DCE-MRI scan providing to radiologist a set of files in DICOM format that represents a 4D volume. Then the radiologist visually analyses the whole data-set in order to provide a diagnosis.

Clinical Scenario (2/2)

The radiologist can send the MRI to a processing server on which runs a full automatic Computer Aided Detection/Diagnosis (CAD) for breast cancer analysis. The server responds with segmented regions (ROI) and diagnosis that the doctor can evaluate and eventually confirm by producing the final diagnosis.





A typical CAD system

Volume Extraction → **Pre-processing** → **ROI Detection** → **ROI Classification**

- **Volume Extraction**
  - The whole 4D volume is created from the DCE-MRI data.
    - 3 Spatial dimension
    - 1 Temporal dimension
- **Preprocessing**
  - In this stage some image processing techniques are applied with the aim of improving next stages results
- **ROI Detection**
  - At this stage tumour lesions are identified as ROI (Region Of Interest), both malignant and benign
- **Classification**
  - Each ROI is classified according to its staging

My Proposal: BLADeS

- **BLADeS: Breast Lesion Automatic Detection System**
  - Aims to support radiologist through lesion detection and diagnosis stages, suggesting suspect ROIs and therapy assessment.

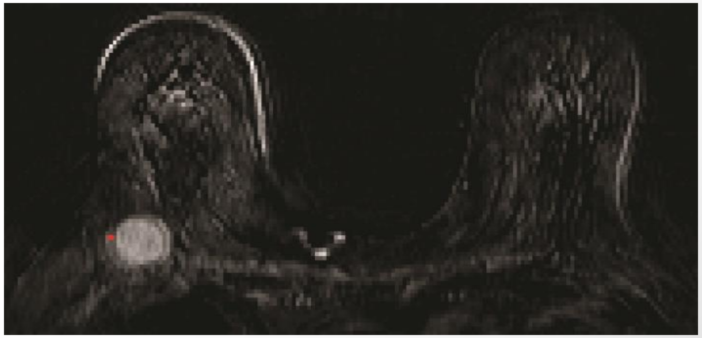
Volume Extraction → **Pre-processing** → **ROI Detection** → **ROI Classification** → **Therapy Assessment**

Pre-processing: **Breast Mask Extraction** → **Motion Correction**

- **Breast mask extraction**
  - Aims to reduce the computational cost of further steps
  - Select only the breast parenchyma
  - Combine fuzzy c-means (FCM) clustering by exploiting 7 automatically extracted anatomical priors.

FCM Clustering → Anatomical Evaluation

- **Motion Correction**
  - Aims to reduce motion artefacts (such as patient breathing or involuntary movements).
  - Relies on a novel model-based QI.



My Proposal: BLADeS

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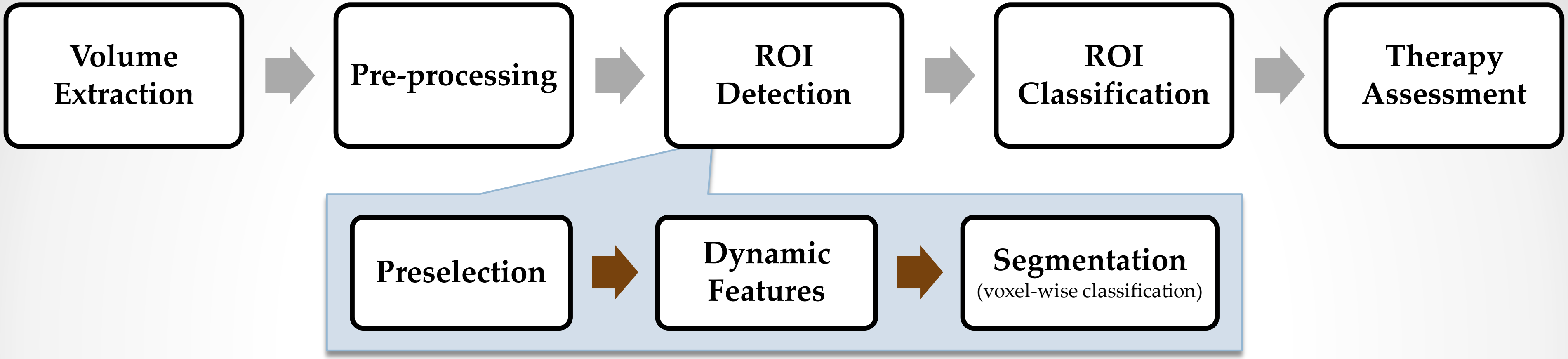

- **ROI Detection**
  - Based on SVM classifier trained on Dynamic features,
  - Each voxel is labelled as: Suspect/not Suspect,
  - The preselection phase strongly improves next stages results by reducing the domain of interest faced in the segmentation (by classification) stage,
  - The union of the connected voxel marked as suspected represents a Region Of Interest (ROI).

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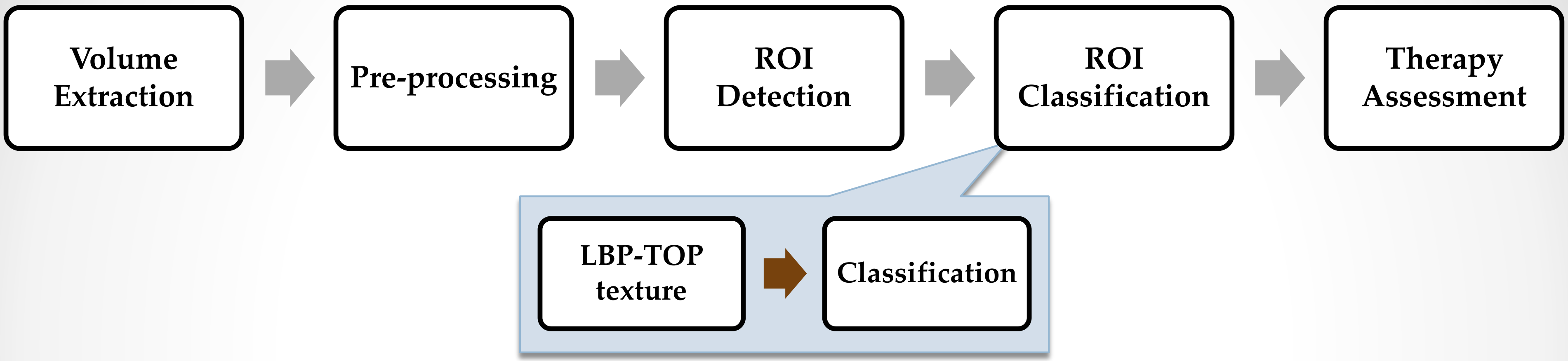

- **ROI Classification**
  - Based on RF classifier trained on Textural features,
  - Each ROI is labelled as: Benignant ROI/Malignant ROI,
  - Local Binary Patterns from Three Orthogonal Planes (LBP-TOP) fuses spatial and temporal texture in an unique descriptor

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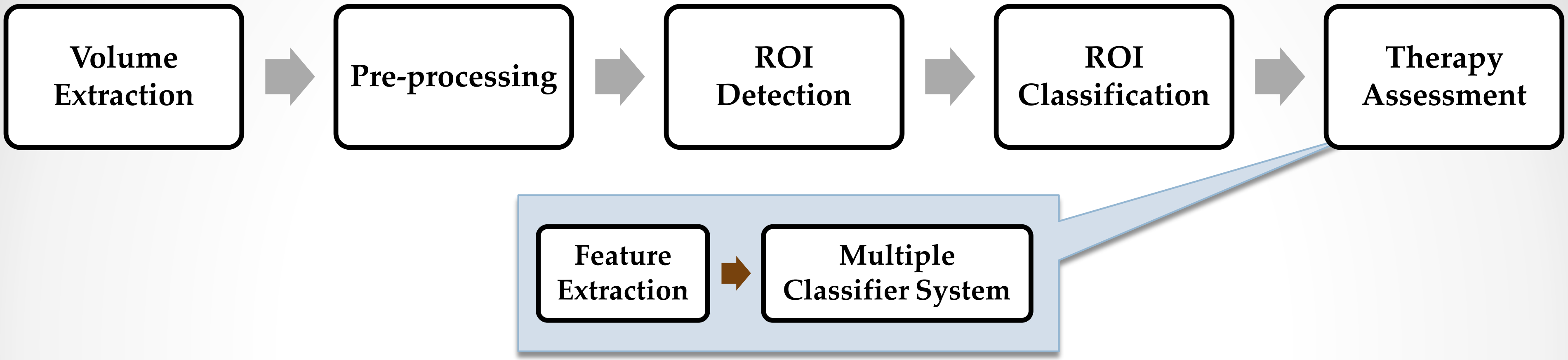
  - Aims to support radiologist through lesion detection and diagnosis stages, suggesting suspect ROIs and therapy assessment.



- **Therapy Assessment**
  - Predict the recurrence of the primary tumour after a surgery treatment,
  - Make use of information available before or during the pre-surgery treatment,
  - Different Feature: Dynamic, Pharmacokinetic, Clinical and Geometrical,
  - Two different classifiers.

My Proposal: BLADeS

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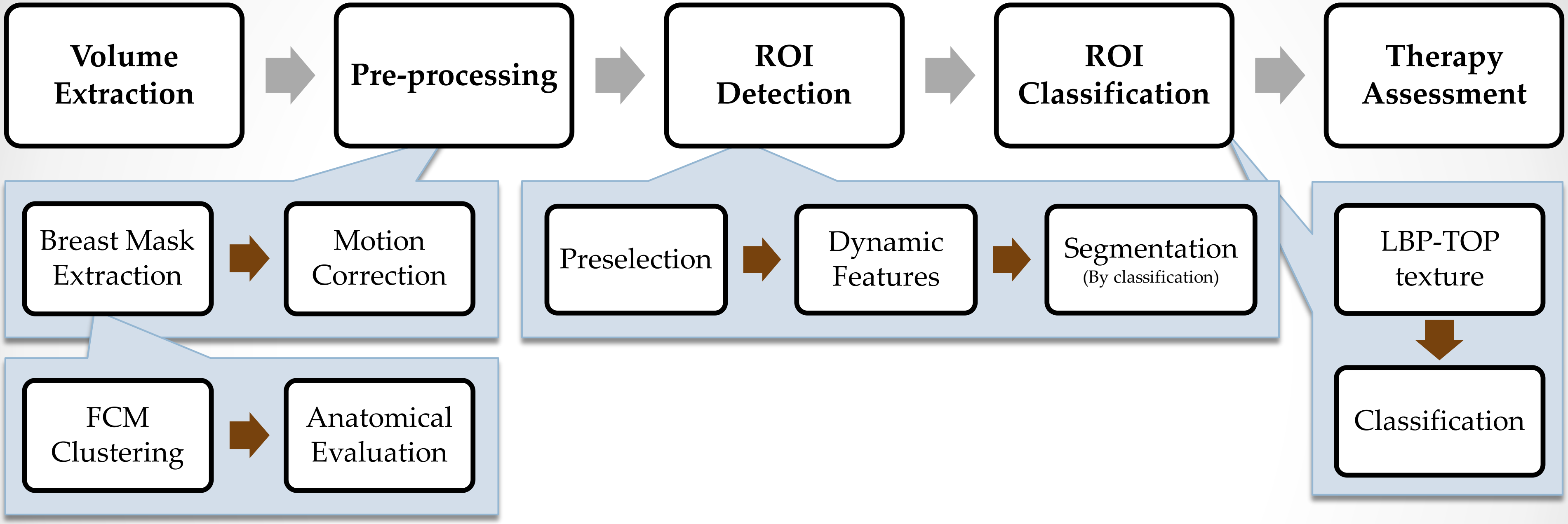


Datasets

- **All the results are evaluated on the following datasets**

	PASCALE (private)	QIN (public)	ISPY1 (public)
N. Patients	42	64	162
Weighting	T1	T1 (fat-sup)	T1 (fat-sup)
Protocol	Flash3D	Flash3D	Flash3D
Mode	Coronal	Sagittal (monolateral)	Sagittal (monolateral)
Scanner	1.5T	1.5T	1.5T
TR/TE	8.9 / 4.76 ms	8 / 4.2 ms	≤ 20 / 4.5 ms
Flip Angle	25 deg	20 deg	≤ 45 deg
FoV	370x185 mm^2	18-20x18-20 cm^2	16-18x16-18 cm^2
Matrix	256x128 px^2	256x192 px^2	≥ 256x192 px^2
Pixel Size	1.445x1.445 mm^2	0.70x0.94 mm^2	≤ 1x1 mm^2
Thickness	2 mm	1.4 mm	1.5-2.5mm
Acquisition Time	56 s	18.2 s	4.5-5 min
Time points	1 pre + 9 post	1 pre + 32 post	1-2 pre + 3-7 post

Breast Mask Extraction

Motion Correction

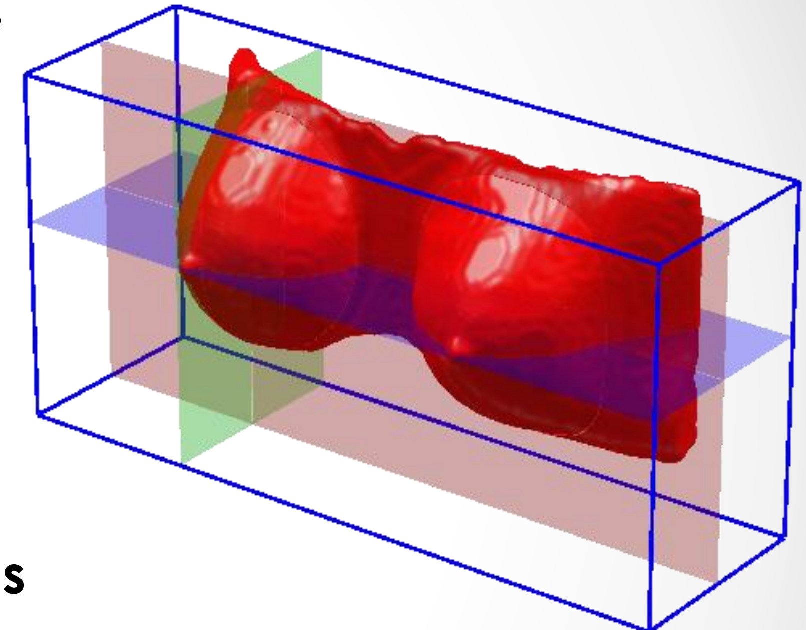
ROI Detection

ROI Classification

Therapy Assessment

Breast Mask Extraction (1/4)

- **Mayor issues in breast mask extraction:**
  - Pectoral Muscle segmentation
  - Lesions that lies on the anatomical structure can change the signal intensity
- **Our proposal**
  - Fuzzy C-means (FCM)
  - Anatomical key-points

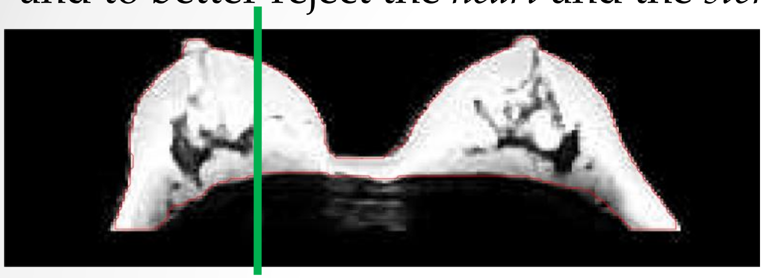


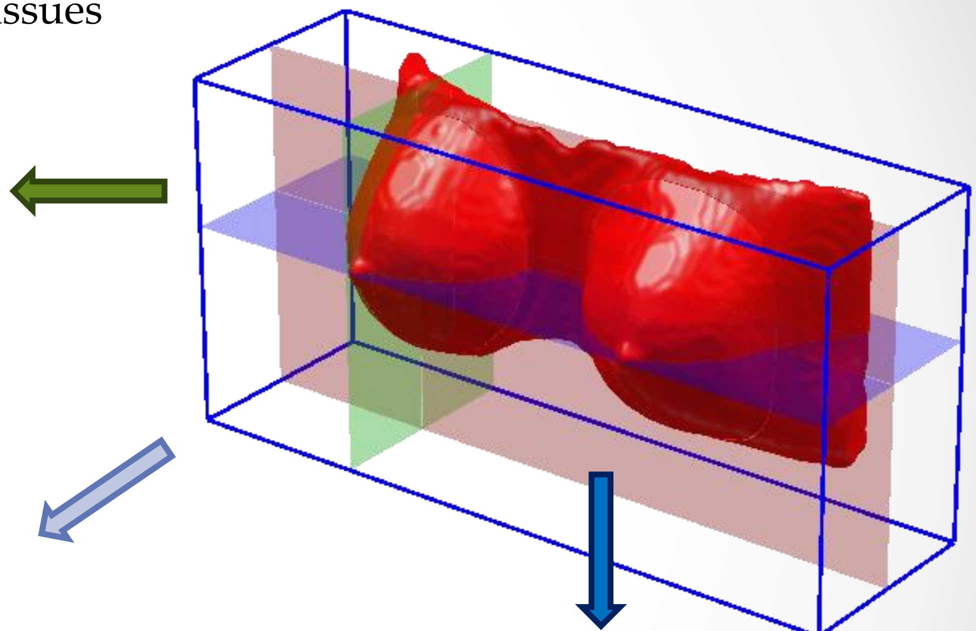
- We extract **3 different FCM** volumes.
- Extract FCM **along different projections** helps to enhance specific anatomical features:
  - Extract FCM for each 2D slice of a specific projection
  - Fuse all the 2D slices in a 3D volume

S. Marrone, G. Piantadosi et al. . Breast segmentation using Fuzzy C-Means and anatomical priors in DCE-MRI" In ICPR2016

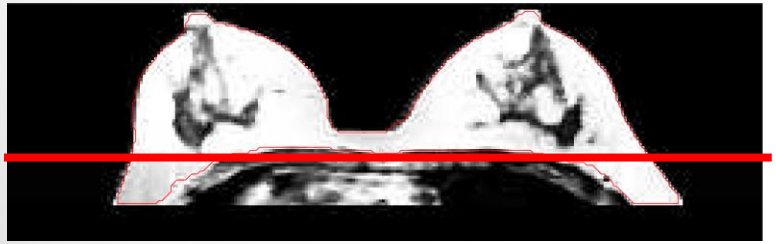
Breast Mask Extraction (2/4)

Sagittal FCM: is able to better enhance the *armpits* cavities and to better reject the *heart* and the *sternum* tissues

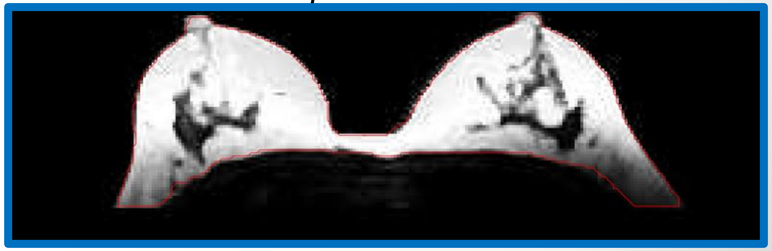




Coronal FCM: easily detects the *breast-air boundary*, but shows a very high enhancement of *pectoral muscle* and *heart*.



Transversal FCM: the *pectoral muscle* edges are sharp, but fails the *armpits* cavities estimation.



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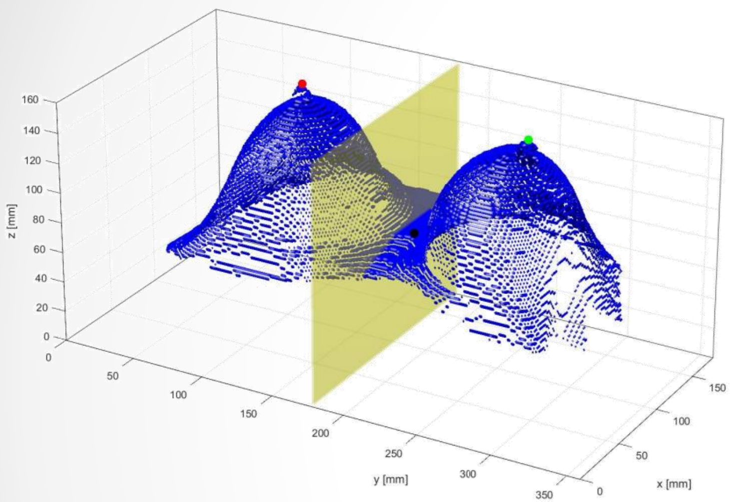
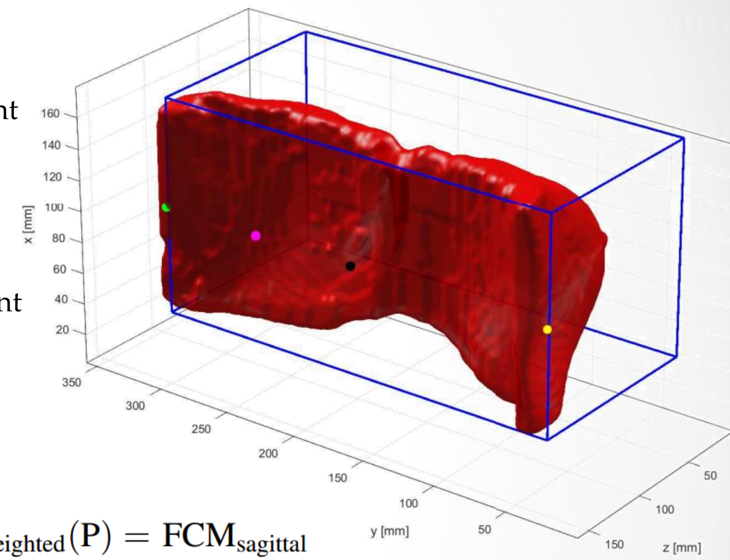
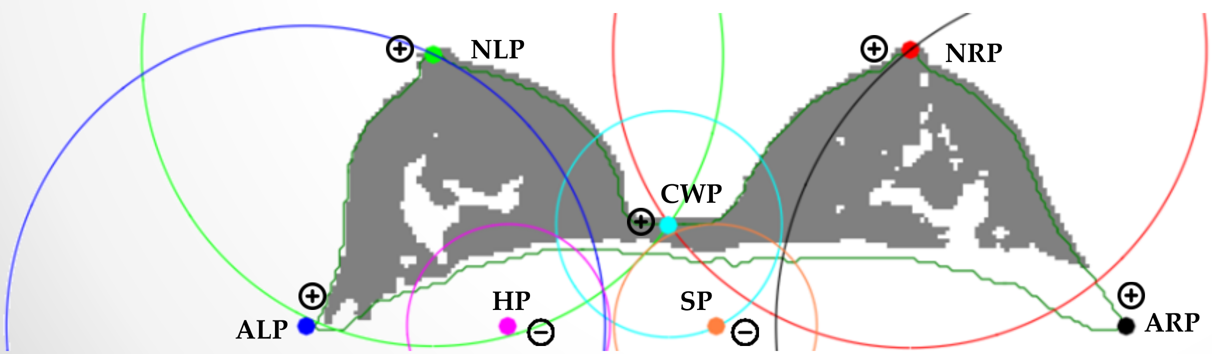
Breast Mask Extraction (3/4)

- Combines the 3 Fuzzy C-Means (FCM) clustering
  - According to the distance (action radius) with respect to seven auto-evaluated key-point (anatomical priors)



- 2 x Nipples (+)
  - **NRP**: Right Nipple Point
  - **NLP**: Left Nipple Point
- Chest Wall (+)
- 2 x Armpits (+)
  - **ARP**: Right Armpit Point
  - **ALP**: Left Armpit Point
- Sternum (-)
- Heart (-)





$$
\begin{aligned}
\mathrm{FCM}_{\mathrm{weighted}}(\mathrm{P}) = \mathrm{FCM}_{\mathrm{sagittal}} &+ \mathrm{FCM}_{\mathrm{frontal}} \cdot \mathrm{kpi}(\mathrm{NRP}, \mathrm{NRPr}, \mathrm{P}) \\
&+ \mathrm{FCM}_{\mathrm{frontal}} \cdot \mathrm{kpi}(\mathrm{NLP}, \mathrm{NLPr}, \mathrm{P}) \\
&+ \mathrm{FCM}_{\mathrm{sagittal}} \cdot \mathrm{kpi}(\mathrm{ARP}, \mathrm{ARPr}, \mathrm{P}) \\
&+ \mathrm{FCM}_{\mathrm{sagittal}} \cdot \mathrm{kpi}(\mathrm{ALP}, \mathrm{ALPr}, \mathrm{P}) \\
&+ \mathrm{FCM}_{\mathrm{transversal}} \cdot \mathrm{kpi}(\mathrm{CWP}, \mathrm{CWPr}, \mathrm{P}) \\
&- \mathrm{FCM}_{\mathrm{frontal}} \cdot \mathrm{kpi}(\mathrm{SP}, \mathrm{SPr}, \mathrm{P}) \\
&- \mathrm{FCM}_{\mathrm{frontal}} \cdot \mathrm{kpi}(\mathrm{HP}, \mathrm{HPr}, \mathrm{P})
\end{aligned}
$$

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Breast Mask Extraction (4/4)

Methodology	Acc.	Sen.	Spe.	Dice Coeff.	Coverage Min.	Coverage Avg.
FCM + Anatomical Priors	**97.9 %**	**95.8 %**	**98.4 %**	**92.7 %**	**100 %**	**100 %**
Geometrical-based [1]	89.5 %	96.3 %	88.7 %	71.0 %	98.7 %	99.9 %
Atlas-based [2]	87.3 %	87.5 %	88.0 %	65.4 %	21.7 %	85.4 %
Geometrical-based [3]	86.4 %	86.5 %	86.8 %	64.2 %	20.4 %	88.5 %
Pixel-based [4]	82.2 %	99.9 %	79.2 %	60.0 %	100 %	100 %

[1] S.Wu et al., "Automated chest wall line detection for whole-breast segmentation in breast MR images", Med. Physics, 40(4):42301, 2013

[2] A. Fooladivanda et al., "Atlas-based automatic breast MRI segmentation using pectoral muscle and chest region model", ICBME, 258, 2014

[3] W. Lu et al., "DCE-MRI segmentation and motion correction based on active contour model and forward mapping", SNPD, 208, 2006

[4] A.Vignati et al., "Performance of a fully automatic lesion detection system for breast DCE-MRI", J. Magnetic Resonance Imaging, 34(6):1341,2011

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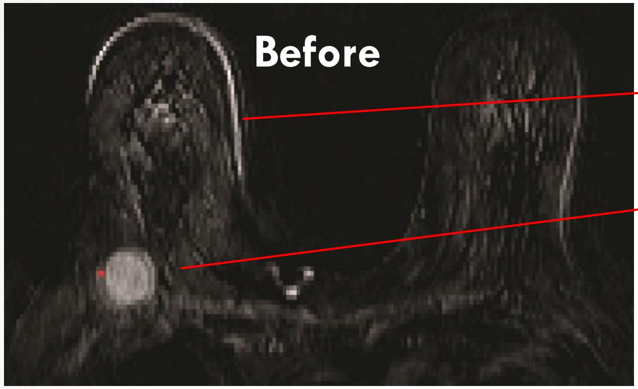
Motion Correction

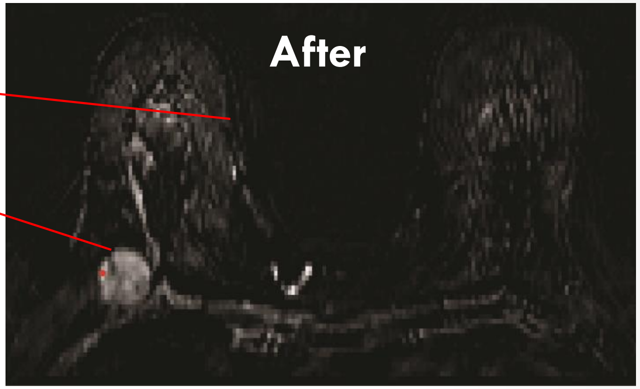
- A MCTs not only attenuate the motion artefacts, but also fix the time course of the time intensity curve by registering the voxels, leading to a better tissue analysis.

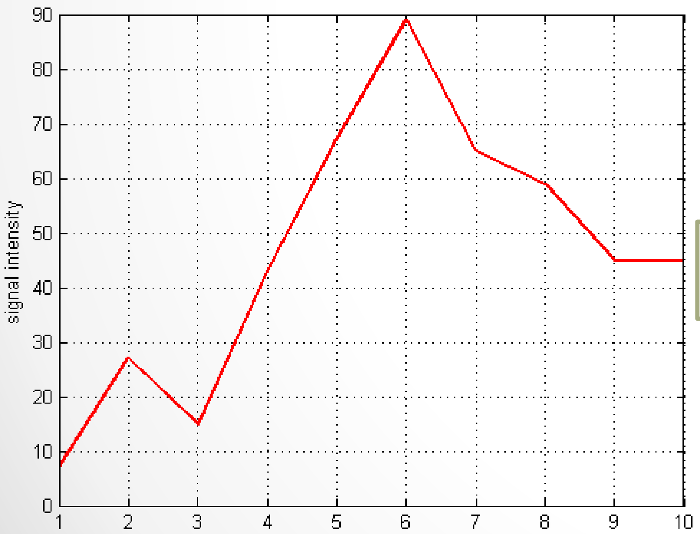


No blurring or ghosting

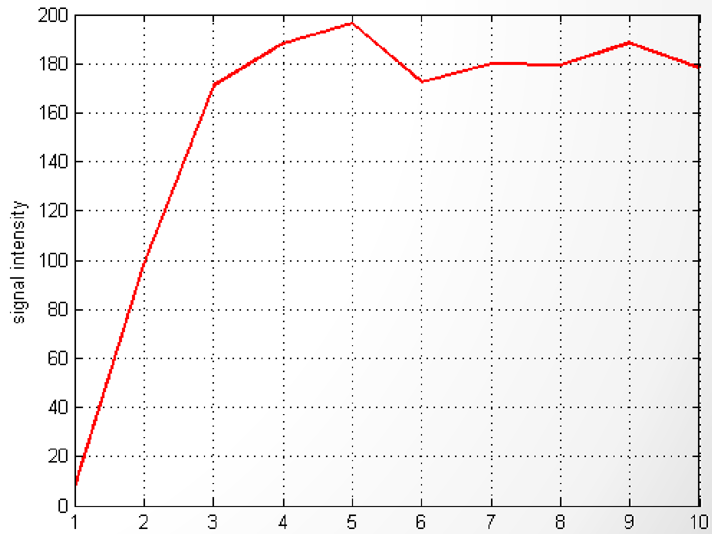
Lesion is well-defined

FFD Motion Correction





TIC curves better fit the physiological behaviour



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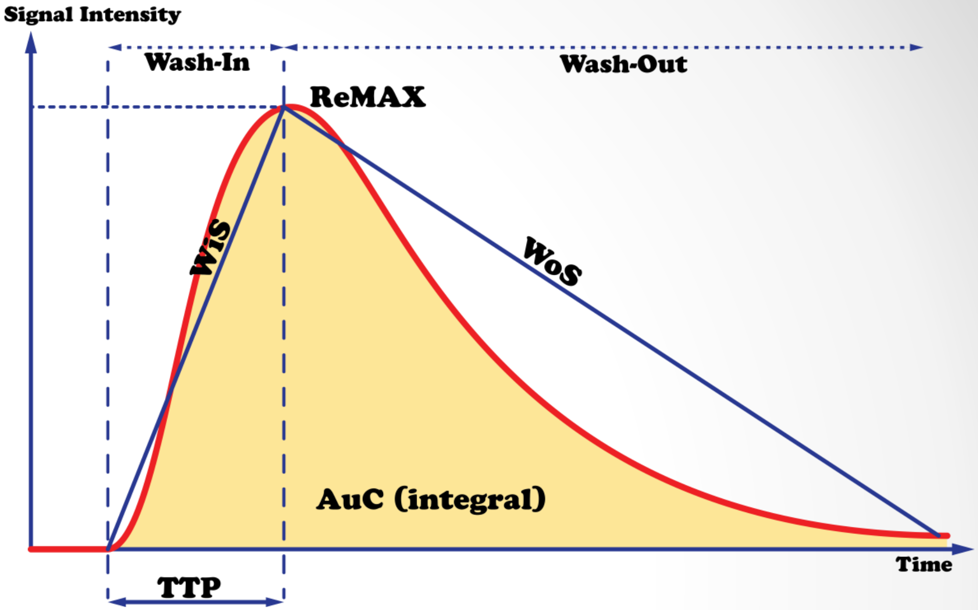
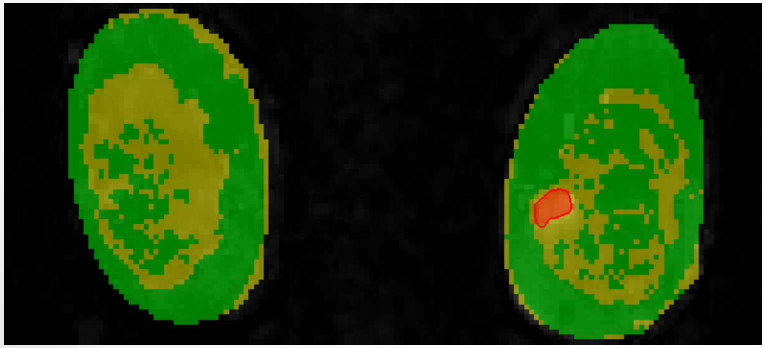
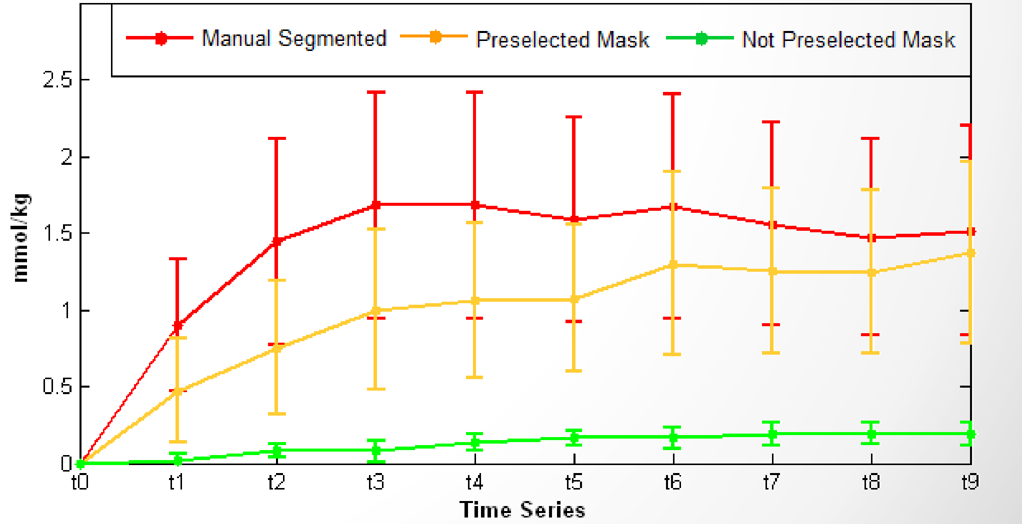
ROI Detection (1/2)

- Pixel-by-pixel segmentation (by classification) with use of dynamical features
  - Area under TIC (**AUC**)
  - Relative Enhancement at Maximum Point (**ReMax**)
  - Time To Peak (**TTP**)
  - Wash-In Slope (**WIS**)
  - Wash-Out Slope (**WOS**)



- Effects of pre-selection stage:





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ROI Detection (2/2)

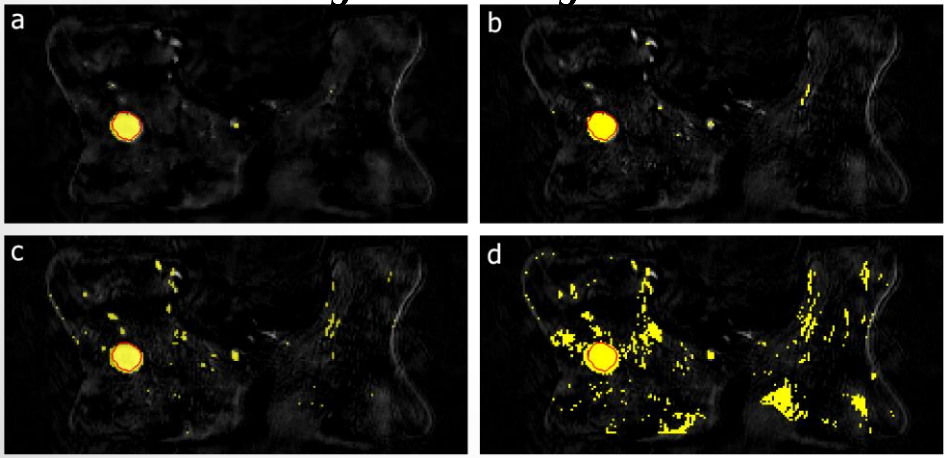
Methodology	Accuracy	Sensitivity	Specificity
a) Our proposal (SVM + Pres)	**98.7 %**	**71.6 %**	**98.9 %**
b) Pixel-Based (Torricelli et al. [1])	98.7 %	25.8 %	99.5 %
c) MLP Based (Fusco et al. [2])	87.0 %	91.0 %	87.0 %
d) Pixel-Based (Fusco et al. [2])	86.6 %	75.4 %	86.6 %

- Best accuracy
- Acceptable sensitivity for the voxel-based detection (few False Negative mostly at the edges)

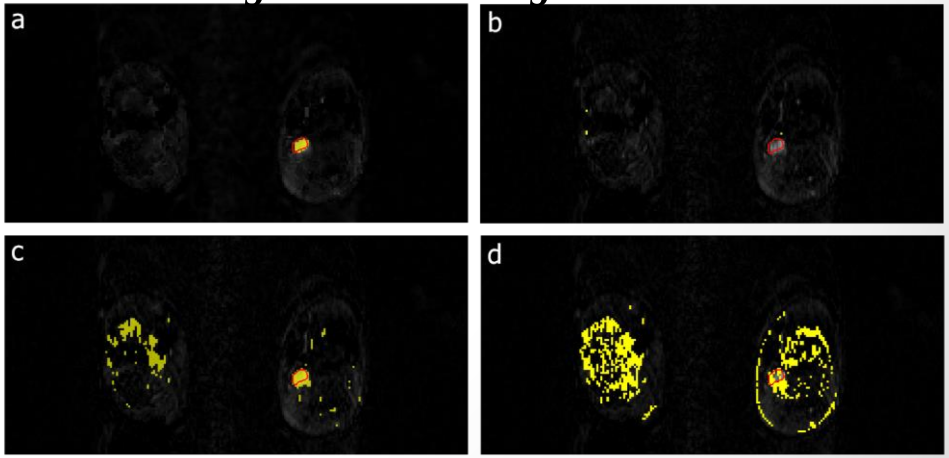
[1] Torricelli, P., et al.: "Gadolinium-enhanced MRI with dynamic evaluation in diagnosing the local recurrence of rectal cancer", Abdom Imaging 28:1927 (2003)

[2] Fusco, R., et al.: "A Multiple Classifier System for Classification of Breast Lesions Using Dynamic and Morphological Features in DCE-MRI", SSPR & SPR 2012, LNCS 7626, pp. 684-692, (2012)

Benign Lesion Segmentation



Malignant Lesion Segmentation



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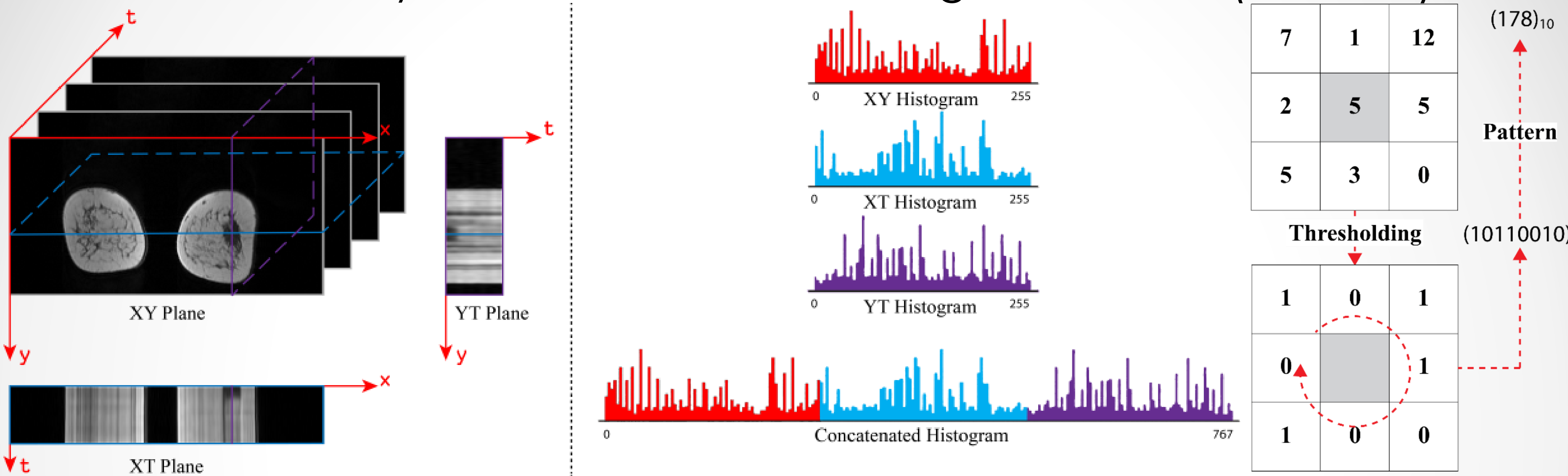
ROI Classification

- 3D Local Binary Pattern from Tree Orthogonal Planes (LBP-TOP)



Authors	Methodology	Accuracy	Sensitivity	Specificity
Our proposal	**LBP-TOP + Random Forest**	**84.6 %**	**80.0 %**	**90.9 %**
	Dynamic features + Naive Bayes	65.4 %	80.0 %	45.5 %
Fusco et al. [1]	Morphological features + Decision Tree	65.4 %	53.3 %	81.8 %
	Dynamic & Morphological features + Multiple Classifier System	69.2 %	86.7 %	45.5 %
Glaßer et al. [2]	Morphological & Clinical features + Decision Tree	61.5 %	93.3 %	18.2 %

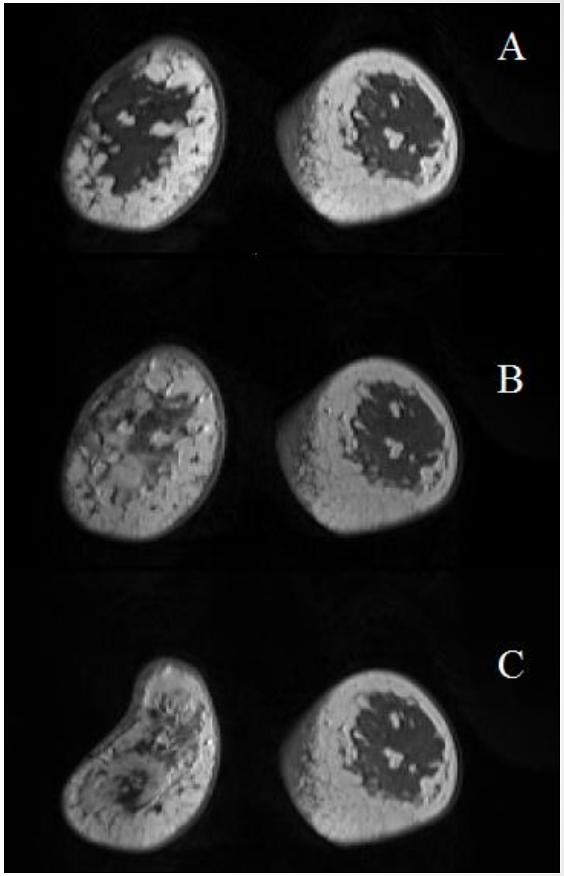
[1] Fusco, R., et al.: "A Multiple Classifier System for Classification of Breast Lesions Using Dynamic and Morphological Features in DCE-MRI", SSPR & SPR 2012, LNCS 7626, pp. 684-692, (2012)

[2] Glaßer, et al.: "Can we distinguish between benign and malignant breast tumors in DCE-MRI by studying a tumor's most suspect region only?", CBMS 2013, IEEE, pp. 77–82. (2013)

G. Piantadosi et al. - "LBP-TOP for Volume Lesion Classification in Breast DCE-MRI", in ICIAP2015

MCT Quality Evaluation

- **Problem:** how to choose a Motion Correction?
- Our studies showed that **there is no single Motion Correction Technique (MCT)** suitable to handle any kind of motion
- It follows that the MCT should be tailored on a patient and exam basis
- How to compare and choose the most suitable MCT for a given patient DCE-MRI exam?
    - **Traditional similarity indexes** are based on voxel signal intensity $SI(x, y, z, t)$
    - They are **poorly reliable** due to intensity variation caused by the contrast agent course

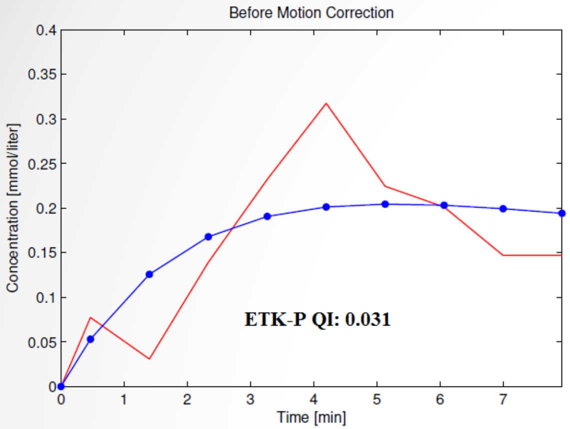


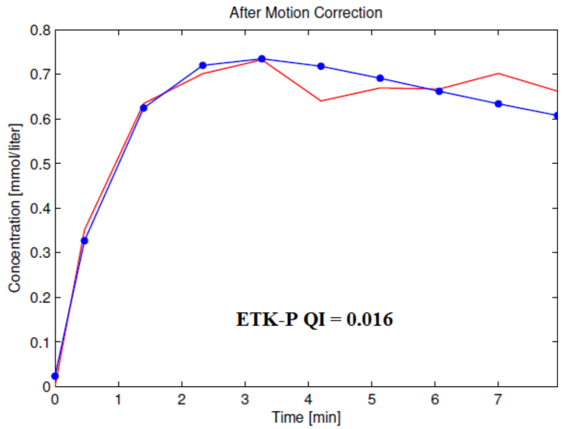
- A) pre-contrast image
- B) post-contrast image
- C) a deformation introduced by an improper MCT

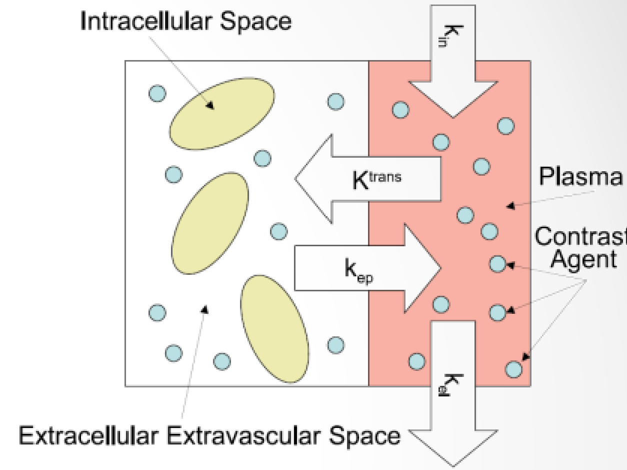
S. Marrone, G. Piantadosi et al. – "A Novel Model-based Measure for Quality Evaluation of Image Registration Techniques in DCE-MRI" in CBMS2014
G. Piantadosi et al. - "Data-driven selection of motion correction techniques in breast DCE-MRI" in MeMeA2015.

Proposed Quality Index

- The contrast agent concentration is fitted to a **Physiologically Based PharmacoKinetic (PBPK)** model solving a non-linear curve-fitting problem in the non-linear least-squares sense







- **Physiologically Based PharmacoKinetic (PBPK) modelling:**
  - **Tofts-Kety (TK) and Extended Tofts-Kety (ETK)**
    - Contrast agent concentration is modelled by the result of convolution between an exponential kernel and an Arterial Input Function (AIF)
  - **Hayton-Brady (HB)**
    - No physiological meaning of the parameters → more flexibility in curve-fitting problem
  - **Gamma Capillary Transit Times (GCTT)**
    - Proposed to unify many of the previous proposed models.

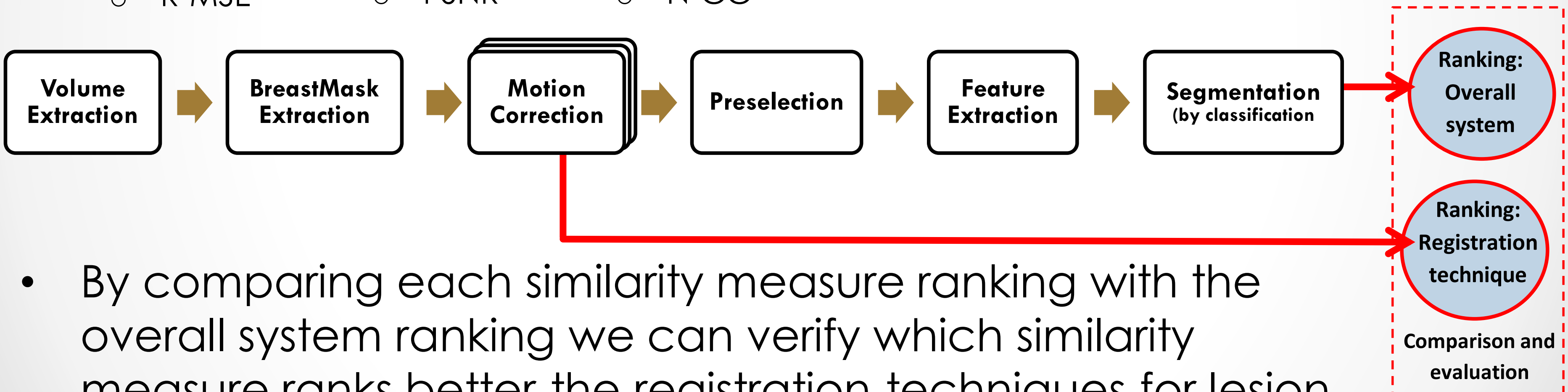
QI family	Underlying Model
HB	Hatyon-Brady
TK-W	Tofts-Kety + Weinmann AIF
TK-P	Tofts-Kety + Parker AIF
ETK-W	Extended Tofts-Kety + Weinmann AIF
ETK-P	Extended Tofts-Kety + Parker AIF
GCTT	Gamma Capillary Transit Times + Parker AIF

- **Proposed Quality Indexes (QIs):**
  - Based on the PBPK models.
  - Different population-averaged AIF
    - Weinmann or Parker

S. Marrone, G. Piantadosi et al. – "A Novel Model-based Measure for Quality Evaluation of Image Registration Techniques in DCE-MRI" in CBMS2014
G. Piantadosi et al. - "Data-driven selection of motion correction techniques in breast DCE-MRI" in MeMeA2015.

QI Results Evaluation

- To evaluate each similarity measure we perform a specific BLADeS execution for each analysed MCTs
  - 2D Affine
  - 3D Affine
  - 3D Non-Rigid
  - Median Filtering
  - ElastiX
- According to segmentation results we have drawn an overall ranking for each registration technique (used as gold-standard).
- Another ranking was obtained using each different similarity measure
  - R-MSE
  - PSNR
  - N-CC



- By comparing each similarity measure ranking with the overall system ranking we can verify which similarity measure ranks better the registration techniques for lesion segmentation purposes.

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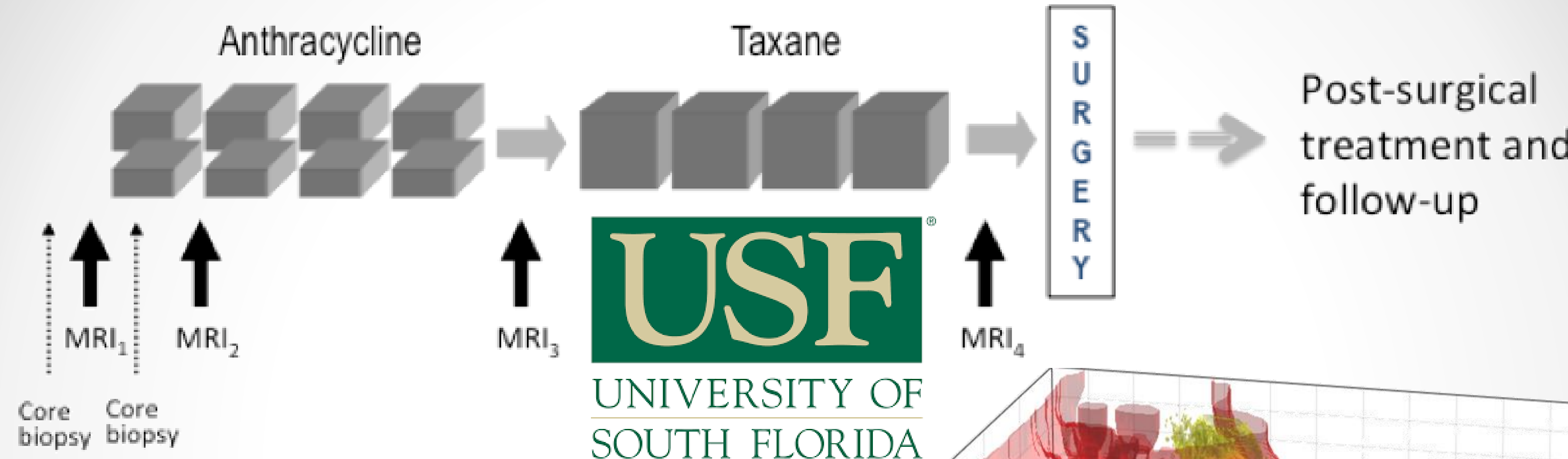
QI Results summary

Pat.	NO	ML	MEDx3	MEDx5	Ru_AC	Ru_AL	Ru_BL	Ru_BC	ElastiX
p1	9°	7°	4°	**1°**	6°	5°	3°	8°	2°
p2	2°	5°	6°	**1°**	4°	4°	8°	7°	3°
p3	5°	4°	3°	9°	6°	**1°**	4°	7°	2°
p4	2°	4°	6°	7°	5°	3°	7°	9°	**1°**
p5	4°	5°	2°	**1°**	4°	6°	8°	8°	3°
p6	**1°**	5°	3°	4°	5°	5°	5°	9°	2°
p30	6°	7°	**1°**	2°	4°	5°	3°	8°	9°
mode	4°	4°	2°	**1°**	6°	2°	7°	9°	3°

QI	Spearman Rank Correlation
R-MSE	6.90%
PSRN	13.56%
N-CC	18.26%
HB	31.31%
GCTT	51.15%
TK-W	55.95%
TK-P	59.17%
ETK-W	58.33%
ETK-P	**73.91%**

S. Marrone, G. Piantadosi et al. – "A Novel Model-based Measure for Quality Evaluation of Image Registration Techniques in DCE-MRI" in CBMS2014
G. Piantadosi et al. - "Data-driven selection of motion correction techniques in breast DCE-MRI" in MeMeA2015.

Therapy Assessment (1/3)



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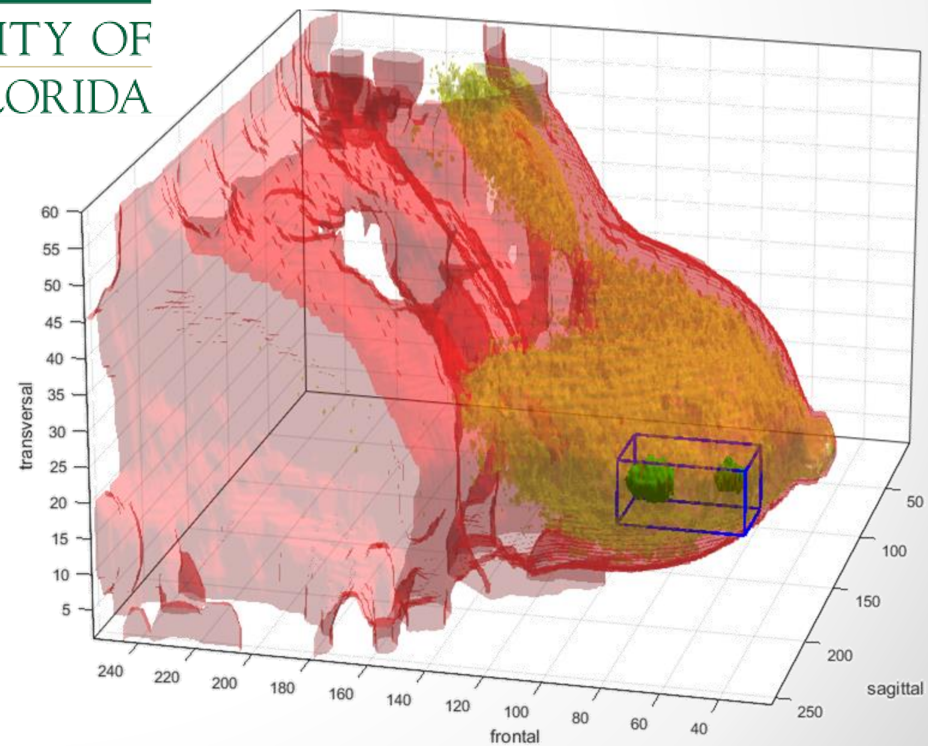


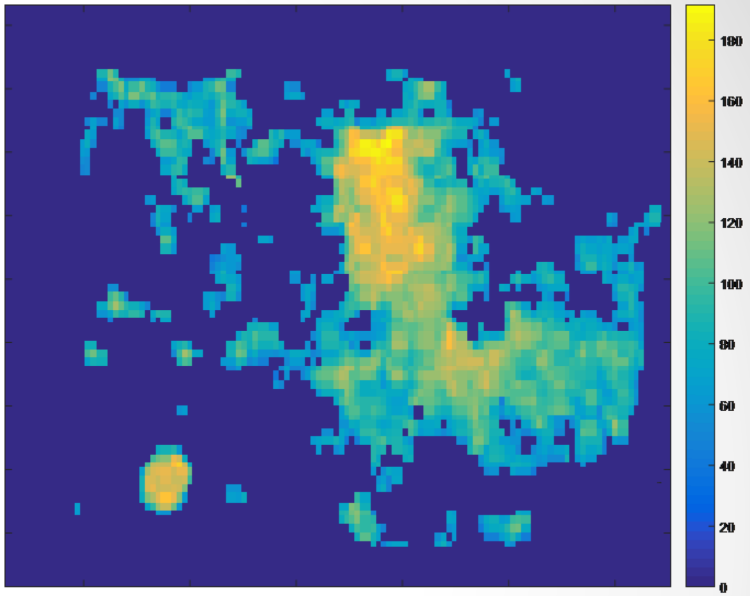
For each patient:

- Up to 4 Time Points (different DCE-MRIs)
- Ground truth
  - Pathological Complete Response (pCR)
  - **Recurrence (Binary class)**
  - Disease Free Survival Time (DFS – in Weeks)

Therapy Assessment (2/3)

The **therapy assessment stage** aims to predict the patient primary tumour recurrence

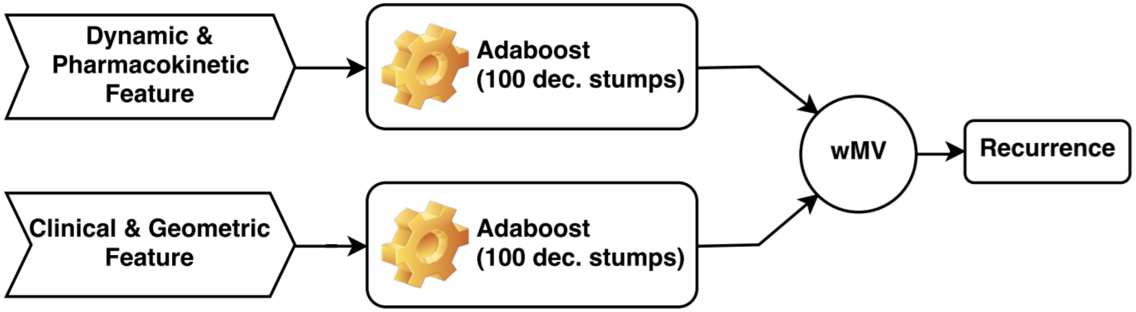
- Different features for each lesion:
  - **Dynamical Features:** the median value of the single feature is considered as representative value for that features in each ROI under examination.
    - #9 Dynamic Features + New proposed features:
      - **Area Under Local Threshold (AULT)**,
      - **Area Under Global Threshold (AUGT)** .



  - **Pharmacokinetic Features:** extracted from the previous depicted Tofts-Kermode (TK) model, a simple compartmental approach.
  - **Morphological Features:** Very simple geometrical features have been used (volumes and diameters). The values before and after the neoadjuvant treatment are considered as features.
  - **Clinicopathologic features:** Directly extracted from the patient records. Represent the clinical status and the pathological condition:
    - Age, Race (categorical), Pathological Complete Response (pCR).

Therapy Assessment (3/3)

- Classification Schema

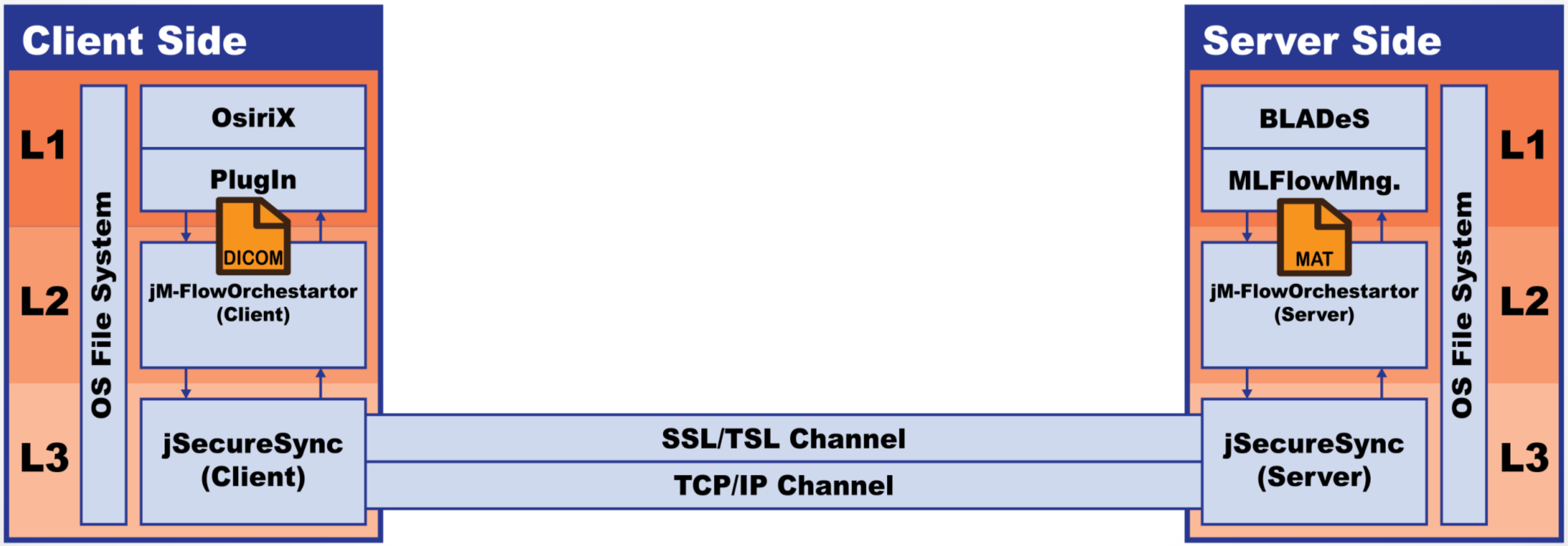


- Results:

Stage	Accuracy	Sensitivity	Specificity	AUC
Dynamic & Pharmacokinetic	76.6 %	59.7 %	83.7 %	75.8 %
Clinical & Geometrical	75.2 %	28.4 %	95.0 %	73.3 %
Combined (wMV)	**77.9 %**	**61.2 %**	**84.9 %**	**79.1 %**

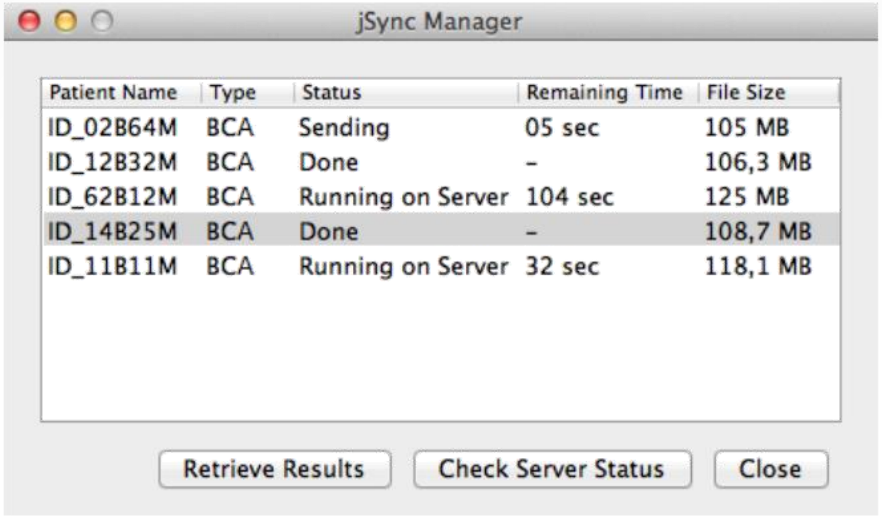
Remote analysis (1/2)

- **Framework for remote processing of huge amount of data**
  - Able to interact with ***different software*** (acquisition and examination software for the medical case study) and instrumentation (different vendors equipment)
  - Context ***scalability*** and ***versatility*** (to meet potential growing of requests)
  - Operational time (a strict constraint such as clinical environment time)
  - Data ***sensitivity*** (privacy must be guaranteed)



G. Piantadosi et al. – "A secure OsiriX plug-in for detecting suspicious lesions in breast DCE-MRI" - ICA3PP 2013
G. Piantadosi et al. - "A secure, scalable and versatile multi-layer client–server architecture for remote intelligent data processing", Journal of Reliable Intelligent Environments - 2015

Remote analysis (2/2)



	Execution time *[s]*		**Throughput**	**Speed-up**
	Mean	**Std.dev.**	*[jobs/s]*	
Local*(1 CPU)	229.34	145.19	15.7	-
Rem.**(1 CPU)	192.60	128.05	18.7	1.2
Rem.**(2 CPU)	199.40	130.41	36.1	2.3
Rem.**(4 CPU)	204.31	130.59	70.5	4.5

* *Tested on a typical OsiriX workstation Apple iMac with Intel Core 2 Duo 2.0 Ghz (3GB RAM)*

** *Tested on a Intel Core i7 64bit Quad Core 3Ghz (12GB RAM)*

G. Piantadosi et al. – "A secure OsiriX plug-in for detecting suspicious lesions in breast DCE-MRI" - ICA3PP 2013

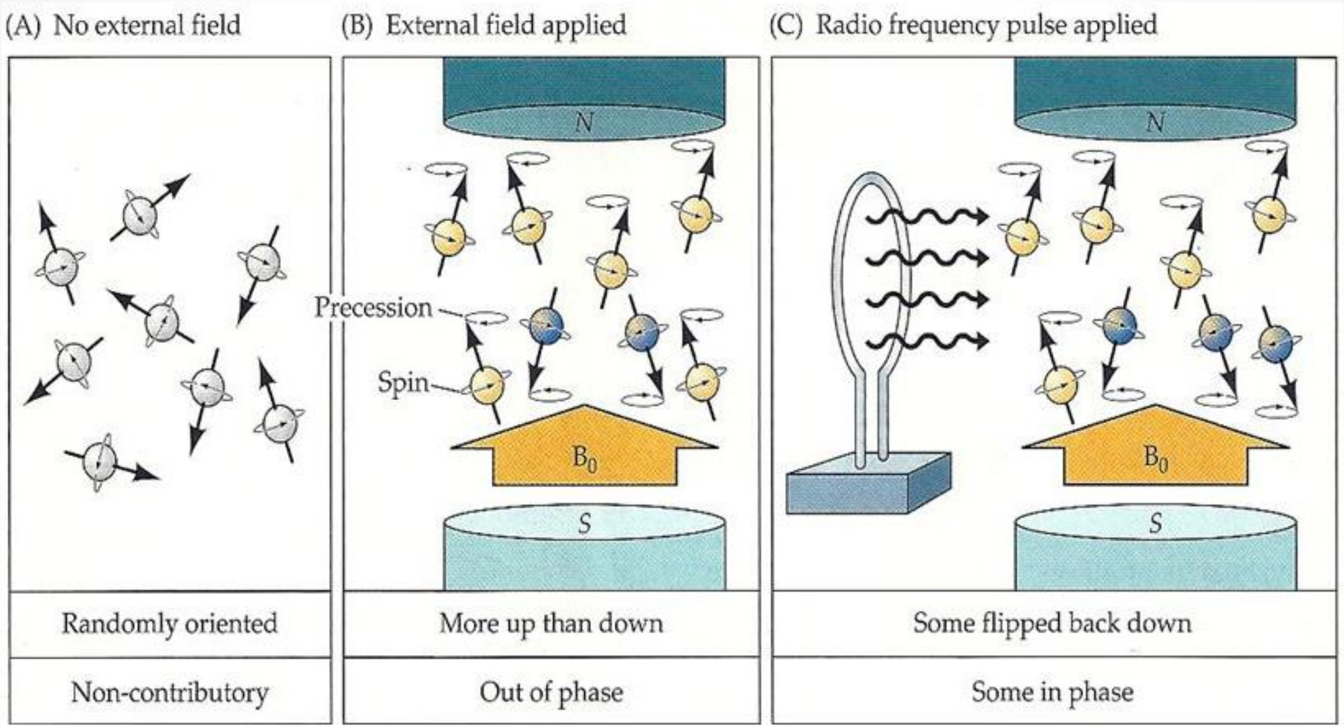
G. Piantadosi et al. - "A secure, scalable and versatile multi-layer client–server architecture for remote intelligent data processing", Journal of Reliable Intelligent Environments - 2015

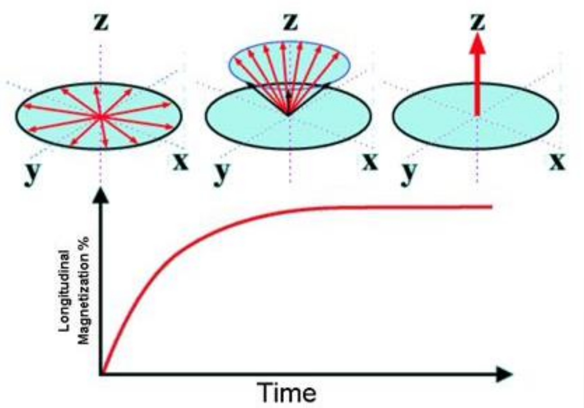
Open Issues

- **Deep Learning approaches**
  - Demonstrated the ability to outperform the classical machine learning approaches in different fields.
  - To the best of our knowledge, very few approaches in DCE-MRI and breast cancer (because of the lack of availability of public data) have been proposed.
- **Protocol-Independent analysis**
  - Improves the reliability of the overall system
  - Handle different cases
    - Bilateral vs. Unilateral
    - Different field of view
    - Different weighting (T1 non fat-sup, T1 fat-sup, T2)
    - Particular case (such as mastectomy, lumpectomy, implants, etc…)
  - Combine DCE-MRI with other diagnostic imaging techniques
    - Diffusion-Weighted Imaging (DWI)
    - Positron Emission Tomography (PET)
    - Computed Tomography (CT)
- **Motion Correction Techniques**
  - Improve the quantitative evaluation of the Motion Correction
  - Develop a new Motion Correction Techniques (model based)

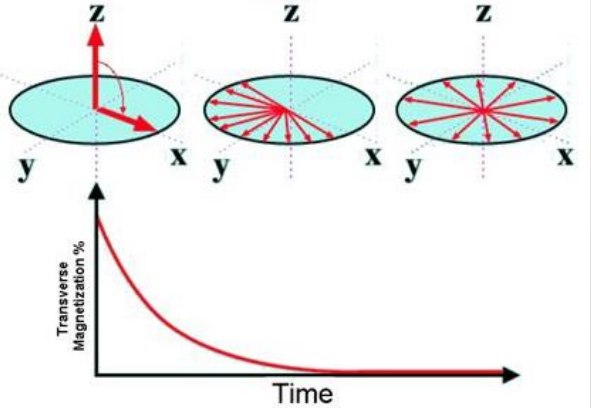
Thank you for your attention!

Physics of MRI (1/2)

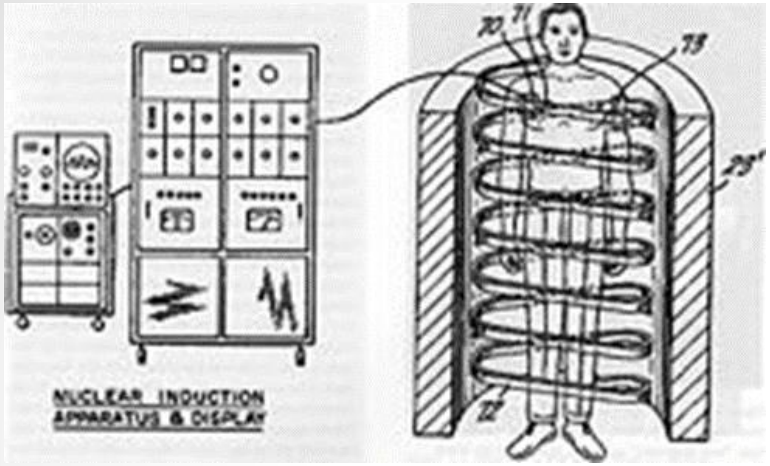




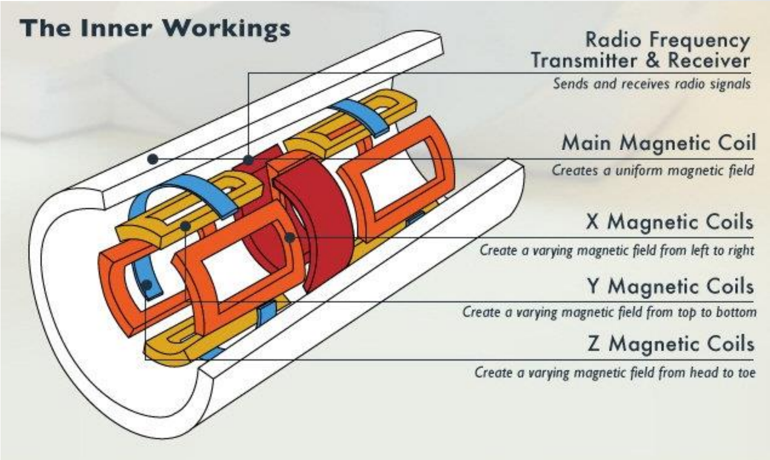
- **Proton Density:**
  - Concentration of protons in the tissue.
- **T1-Relaxation (Recovery):**
  - Recovery of longitudinal Orientation.
- **T2-Relaxation (Dephasing):**
  - Loss of transverse magnetization.

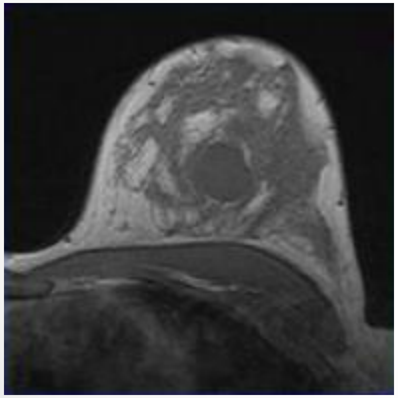


Physics of MRI (2/2)

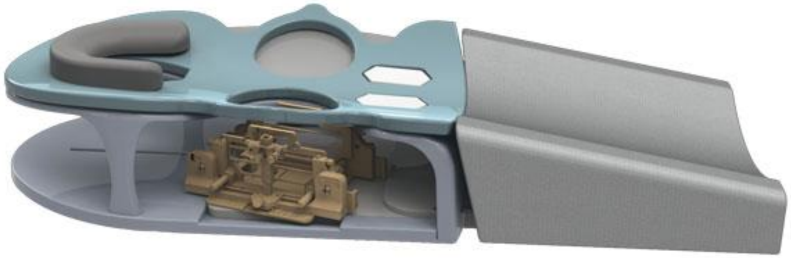


Raymond Damadian (1971)

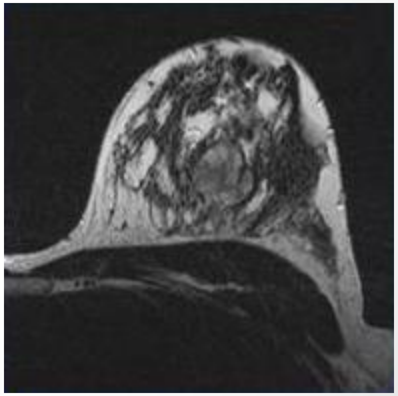




T1



Breast Coils

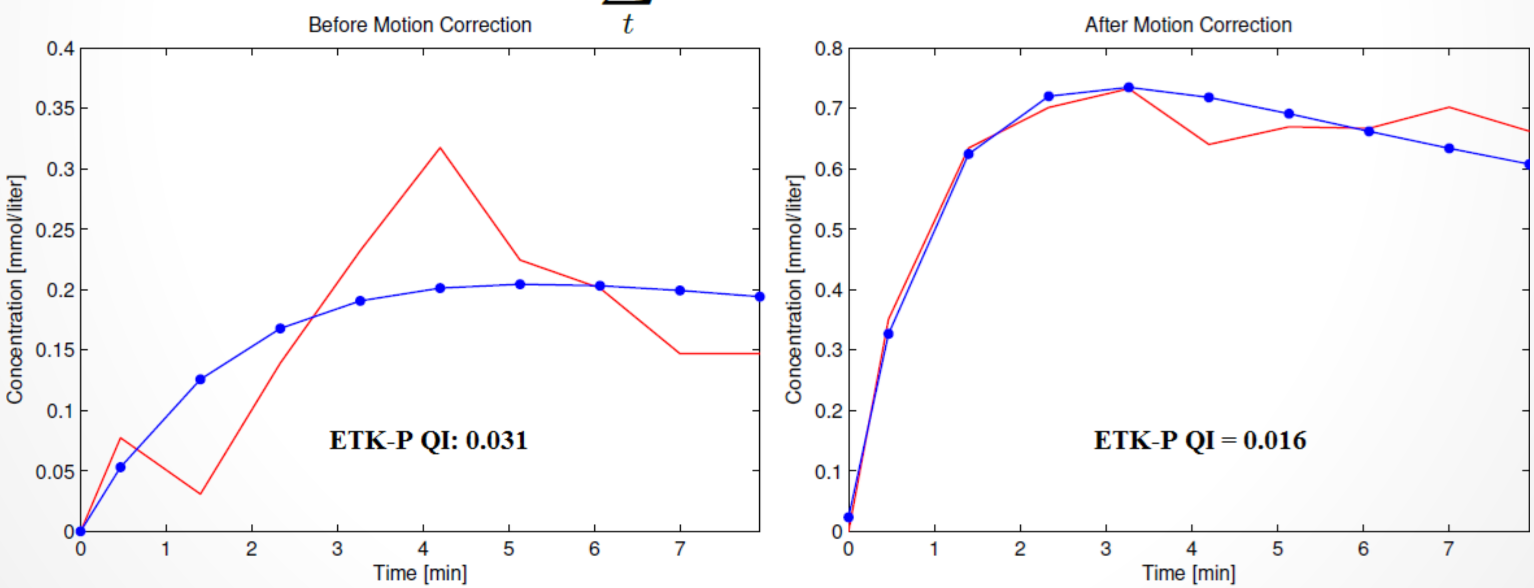


T2

Proposed Quality Index

- The contrast agent concentration is fitted to the breast **Physiologically Based PharmacoKinetic (PBPK)** model solving a non-linear curve-fitting problem in the least-squares sense
- The proposed QI is the median value of the Sum of Squared Errors (SSE) along the time dimension, between the measured and fitted contrast agent concentration $Ct\ (n,t)$, evaluated on a voxel basis. Varying the underlying breast PBPK model, a QI family is obtained

$$\mathtt{QI} = median_n\left(\sum_t (C_t^{fitted}(n,t) - C_t^{measured}(n,t))^2\right)$$



S. Marrone, G. Piantadosi et al. – "A Novel Model-based Measure for Quality Evaluation of Image Registration Techniques in DCE-MRI" in CBMS2014
G. Piantadosi et al. - "Data-driven selection of motion correction techniques in breast DCE-MRI" in MeMeA2015.

Therapy Assessment

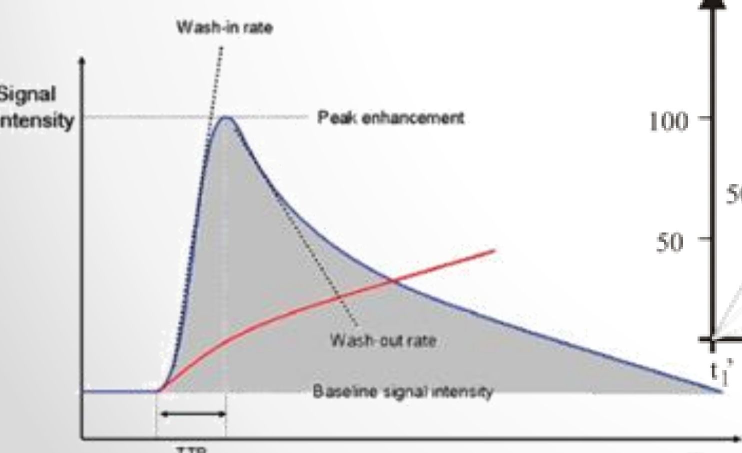
Study Normalization

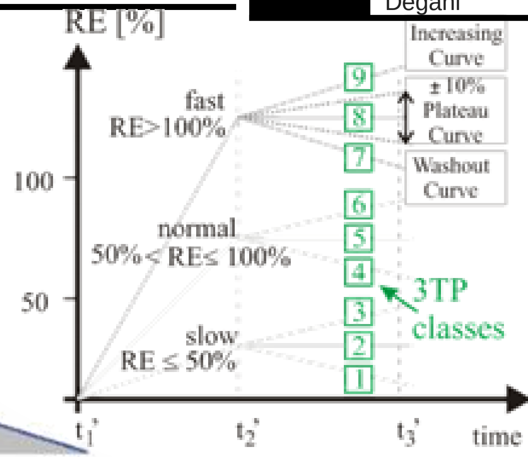
MRI_1	MRI_2	MRI_3	MRI_4	Baseline	Early-treatment	Inter-regimen	Pre-Surgery
X	X	X	X	1	2	3	4
X	X	X		1	2		3
X		X		1			3
X	X		X	1	2		4
X			X	1			4

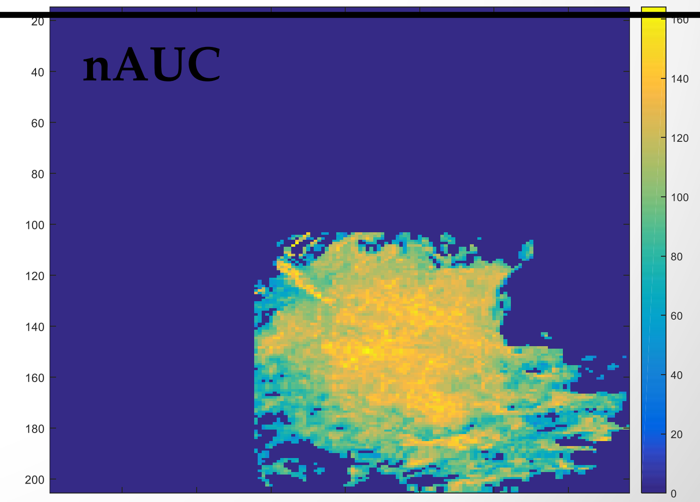
Feature Extraction

	Feature	Description
PE	Peak Enhancement	PE = $(S_1\text{-}S_0)/S_0$
PIE	Post Initial Enhancement	PIE = $(S_2\text{-}S_1)/S_1$
SER	Signal Enhancement Ratio	SER = $(S_1\text{-}S_0)/(S_2\text{-}S_0)$
AUC	Area Under Curve	Area under TIC Curve (fig1. in grey)
nAUC	Normalized AUC	Normalized AUC (in terms of area) aims to only considering the amount of contrast agent absorbed from the specific tissue.
CT	Curve Type	According to Degani classification
WIS	Wash-In Slope	
WOS	Wash-Out Slope	

	Feature	Description
AUGM	nAUC Under Global Moda	Size % w.r.t the tumor size. Threshold: Moda calculated over all the patients
AULM	nAUC Under Local Moda	Size % w.r.t the tumor size. Threshold: Moda calculated over all the single patient
AUGT	nAUC Under Global Threshold	Size % w.r.t the tumor size. Threshold: Otsu
AULT	nAUC Under Local Threshold	Size % w.r.t the tumor size. Threshold: Moda calculated over all the single
CT%	Volume fraction per each Curve Type of Degani	Size % w.r.t the tumor size for all the Curve Type: CT_1, CT_2, CT_3, CT_4, CT_5, CT_6, CT_7, CT_8, CT_9.



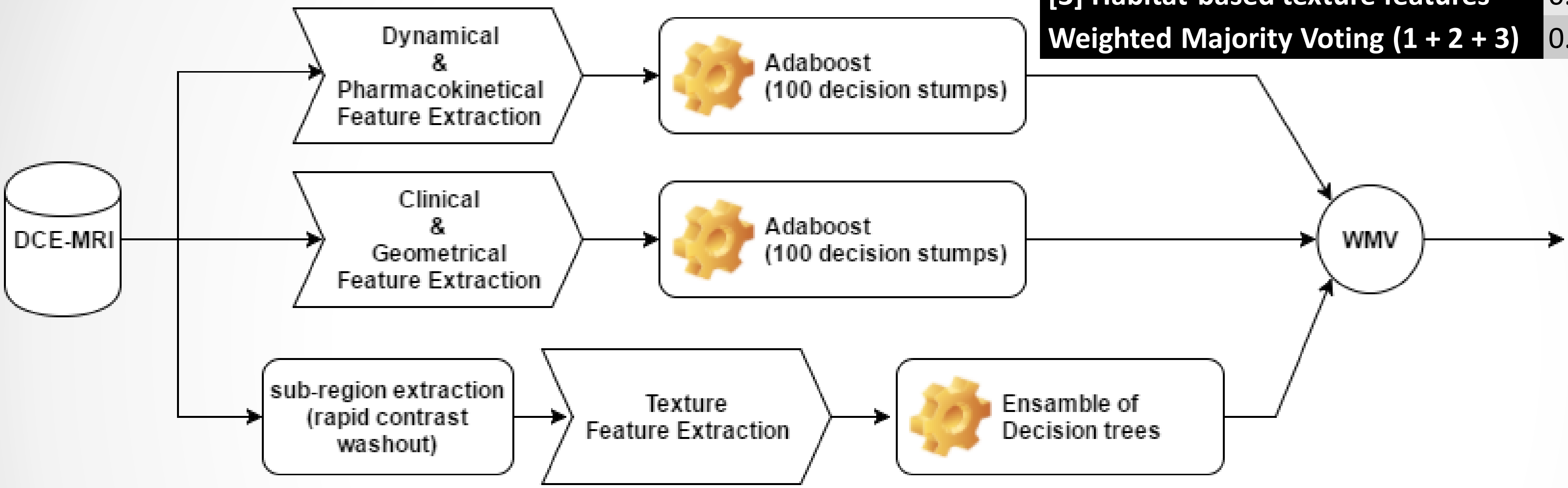




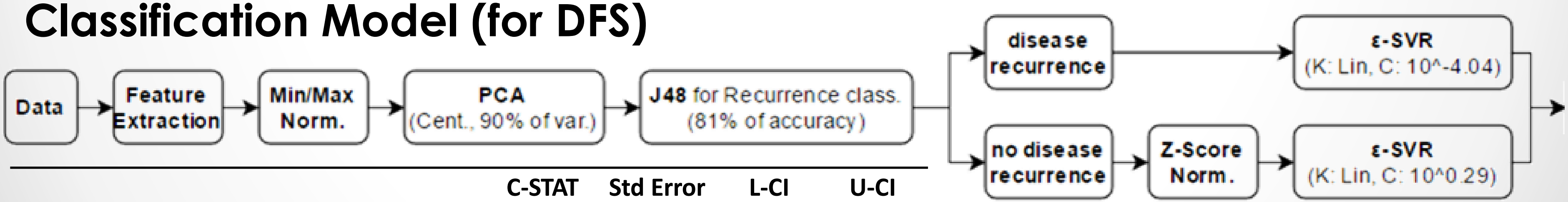
Therapy Assessment

Classification Model (For Recurrence)

Loo-CV	Acc	Sen	Spe	AUC
[1] Dyn. & Pharmacokineical Features	0.766	0.597	0.837	0.758
[2] Clinical & Geom. Features	0.752	0.284	0.950	0.733
Naïve Bayes Combination (1 + 2)	0.779	0.612	0.849	0.791
[3] Habitat-based texture features	0.683	0.438	0.800	0.670
Weighted Majority Voting (1 + 2 + 3)	0.779	0.719	0.807	0.792



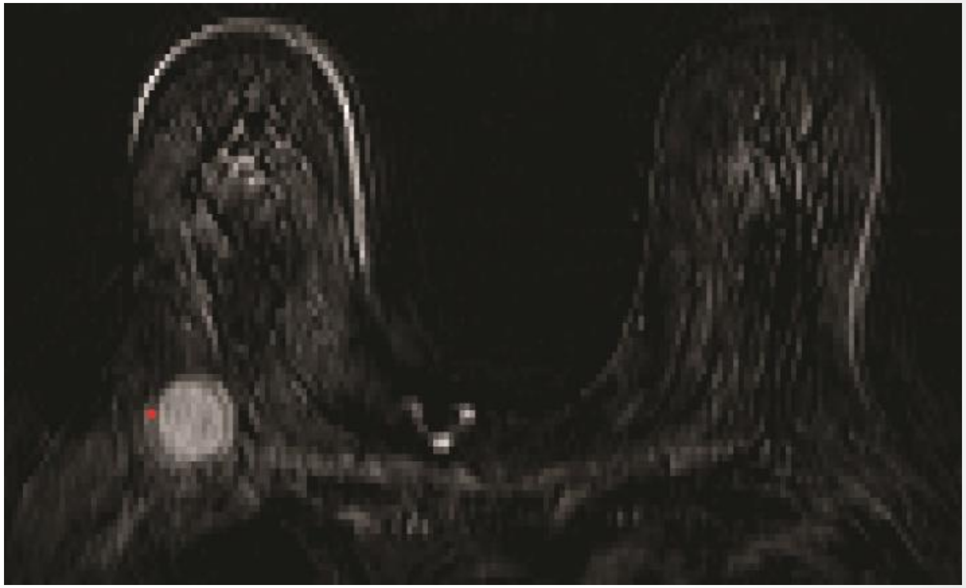
Classification Model (for DFS)



	C-STAT	Std Error	L-CI	U-CI
[1] Dynamical Features	82.4%	0.068	69.1%	95.7%
[2] Feature Selection	82.5%	0.066	69.6%	95.3%
[3] Censor as probability	81.0%	0.068	67.8%	94.3%
Combined [1, 2, 3]	89.7%	0.054	79.1%	100.4%

Motion Artefacts

- Dynamic characteristics of breast examinations make hard to detect
  suspicious ROI due to motion artefacts
  - Involuntary movements (i.e. breathing)
  - Stress restlessness
  - Claustrophobia



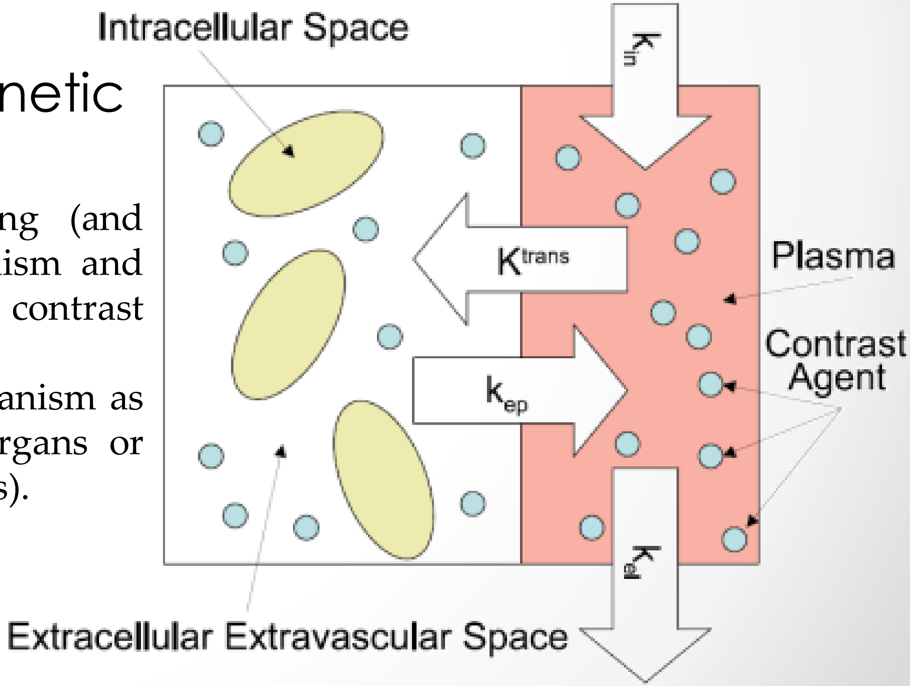
- The problem can occurs in all soft tissues (like breast) and in Dynamic organs (i.e. bowel or heart) examinations

- The motion correction stage aim to remove (or at least reduce) the effects of motion artefacts by means of a Motion Correction Technique (MCT)

S. Marrone, G. Piantadosi et al. . "Automatic Lesion Detection in Breast DCE-MRI" In ICIAP 2013

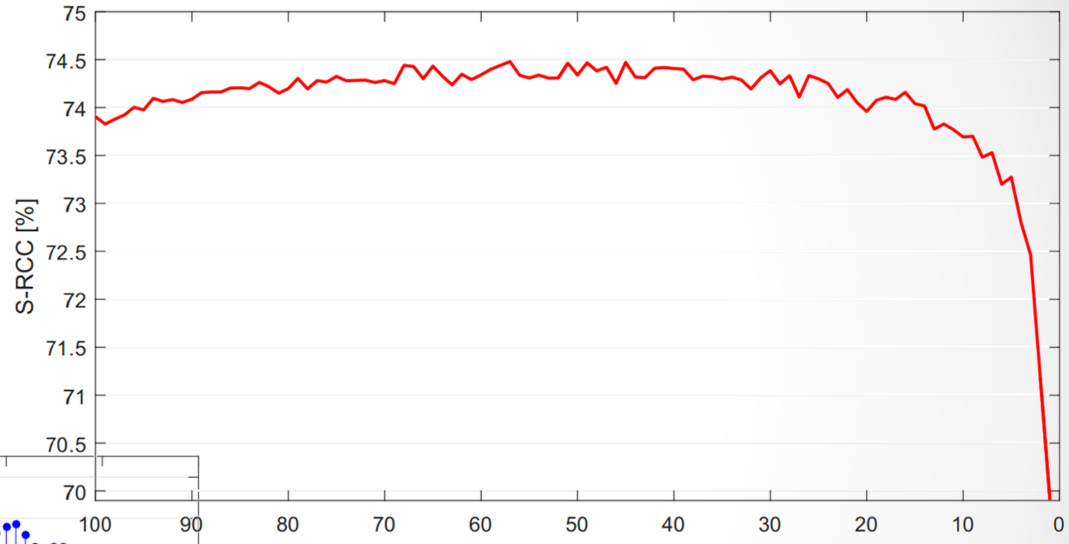
A Model Based Approach

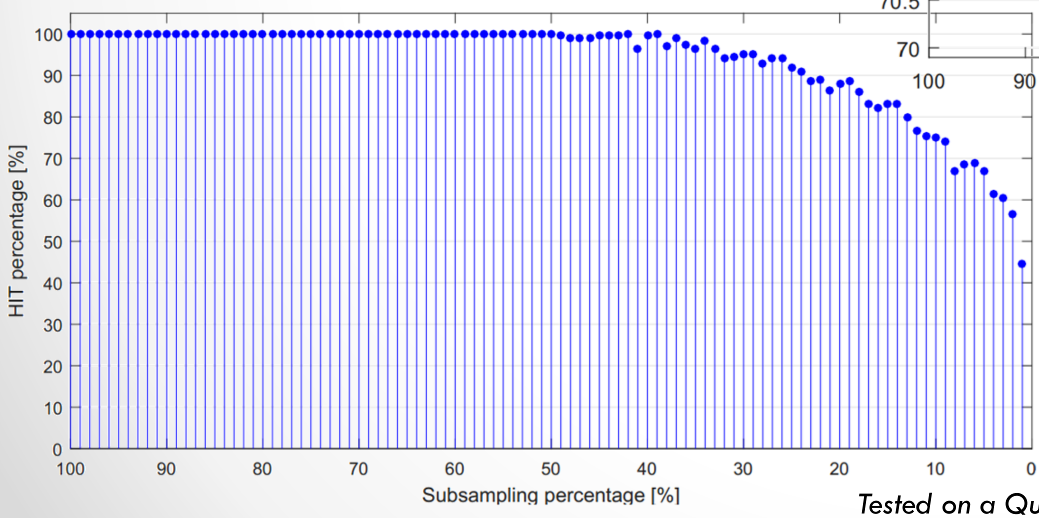
- A model-based Quality Index (QI) for a quantitative evaluation of MCTs in
  breast DCE-MRI
    - The contrast agent course is taken into account using compartmental models to describe the pharmacokinetics of the contrast agents in breast tumours
- The proposed QI can be used for MCTs ranking and then choosing the most suitable one for the specific patient, in a fast, repeatable and reliable manner
- Physiologically Based PharmacoKinetic (PBPK) modelling
    - PBPK modelling is a technique for estimating (and predicting) the absorption, distribution, metabolism and excretion (ADME) of substances (including contrast agents)
    - Compartmental methods models consider an organism as a number of related uniform compartments (organs or tissues) and interconnection (blood or lymph flows).



Results summary (MCT-QI)

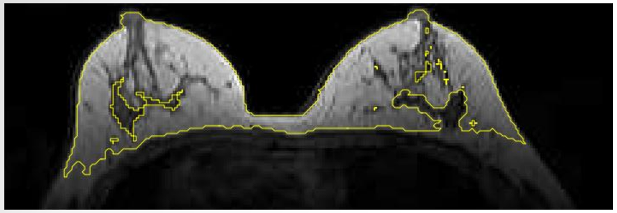
- Each voxel requires a model curve fitting → high computation effort
- We propose to evaluate the model based QI only on a subset of the whole volume
  - 100 % → ≈35000 voxels ~15h
  - 5 % → ≈1700 voxels ~30m
  - 1% → ≈350 voxels ~3m

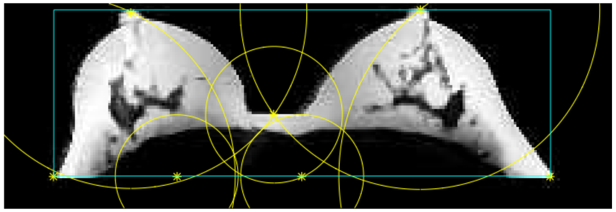


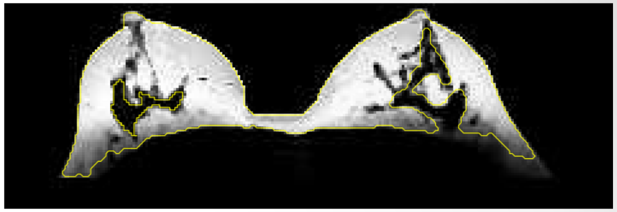


Tested on a Quad Core Xeon 3.0Ghz architecture with 8GB RAM and MATLAB®

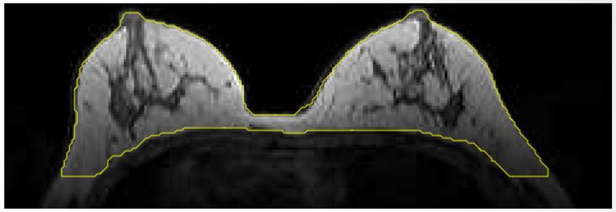
Breast Mask Extraction (4/4)







Methodology	Acc.	Sen.	Spe.	Dice Coeff.	Coverage Min.	Coverage Avg.
FCM + Anatomical Priors	**97.9 %**	**95.8 %**	**98.4 %**	**92.7 %**	**100 %**	**100 %**
Geometrical-based [1]	89.5 %	96.3 %	88.7 %	71.0 %	98.7 %	99.9 %
Atlas-based [2]	87.3 %	87.5 %	88.0 %	65.4 %	21.7 %	85.4 %
Geometrical-based [3]	86.4 %	86.5 %	86.8 %	64.2 %	20.4 %	88.5 %
Pixel-based [4]	82.2 %	99.9 %	79.2 %	60.0 %	100 %	100 %



[1] S.Wu et al., "Automated chest wall line detection for whole-breast segmentation in sagittal breast MR images", Medical Physics, 40(4):42301, 2013

[2] A. Fooladivanda et al., "Atlas-based automatic breast MRI segmentation using pectoral muscle and chest region model", ICBME, 258, 2014

[3] W. Lu et al., "DCE-MRI segmentation and motion correction based on active contour model and forward mapping", SNPD, 208, 2006

[4] A.Vignati et al., "Performance of a fully automatic lesion detection system for breast DCE-MRI", J. Magnetic Resonance Imaging, 34(6):1341,2011

S. Marrone, G. Piantadosi et al. . Breast segmentation using Fuzzy C-Means and anatomical priors in DCE-MRI" In ICPR2016