Shallow and deep learning representations for quantifying spatial heterogeneity in tumours from DCE-MRI

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CANCER RESEARCH UK

CCP-EM

EPSRC
Engineering and Physical Sciences Research Council

UNIVERSITY OF OXFORD

Science & Technology Facilities Council

Presentation outline

1. **The problem**

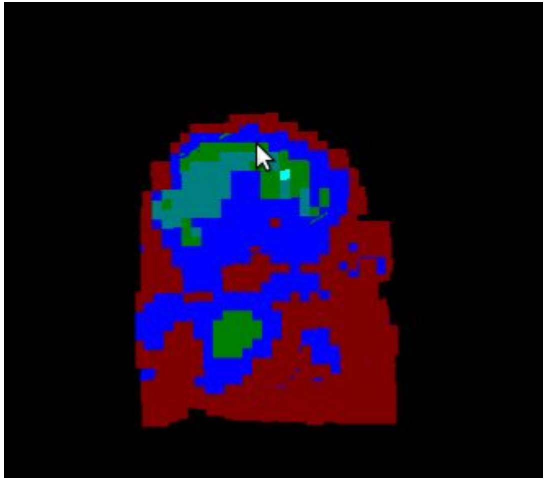
2. **The question**

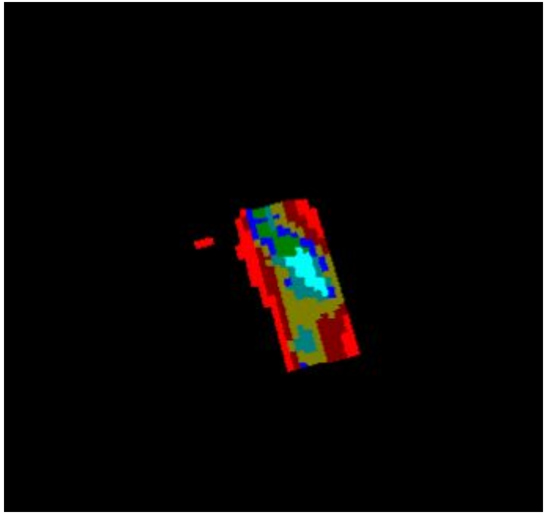
3. **Trial study:**
   3.1. shallow image representations

4. **Methods**:
   4.1. shallow image representations
   4.2. deep image representations

5. **Results**:
   5.1. pre-clinical: tumour progression
   5.2. clinical: response to therapy

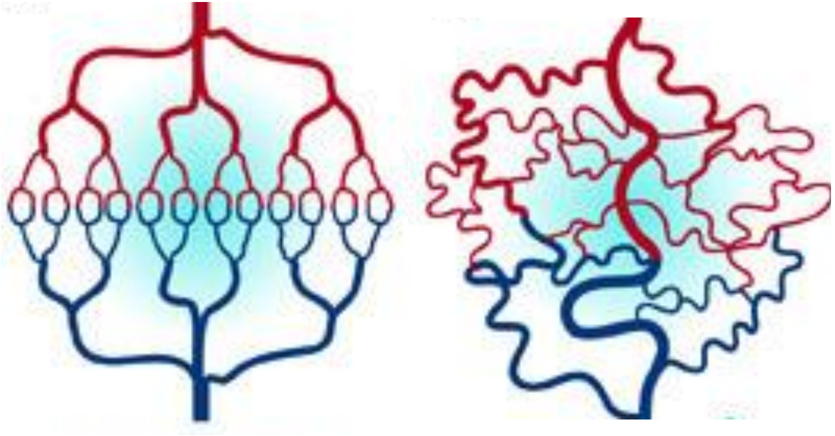
6. **Cryo-EM?**



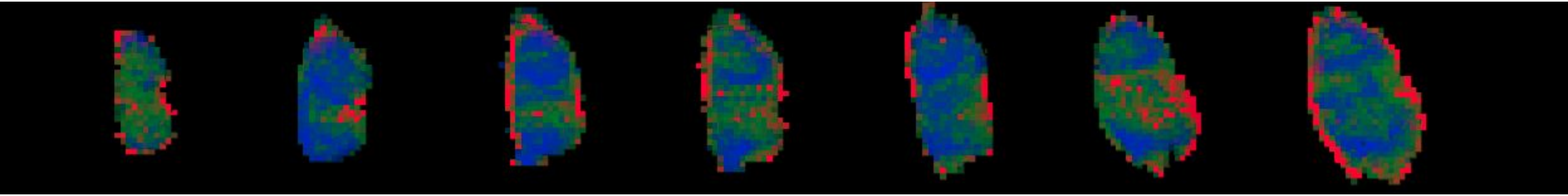


1. The problem
Tumours and heterogeneity

- cancerous tumours are characterized by an increase in heterogeneity
    - ✶ heterogeneity - variation or non-uniformity in composition

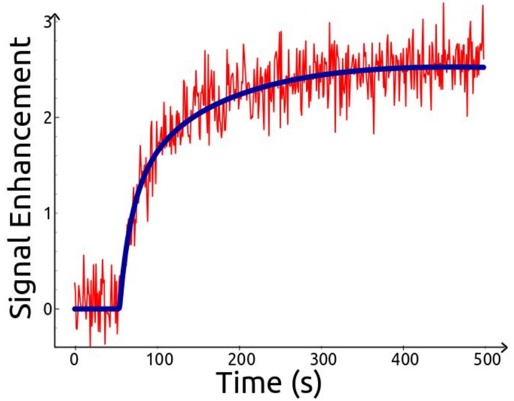


normal vasculature   tumour vasculature

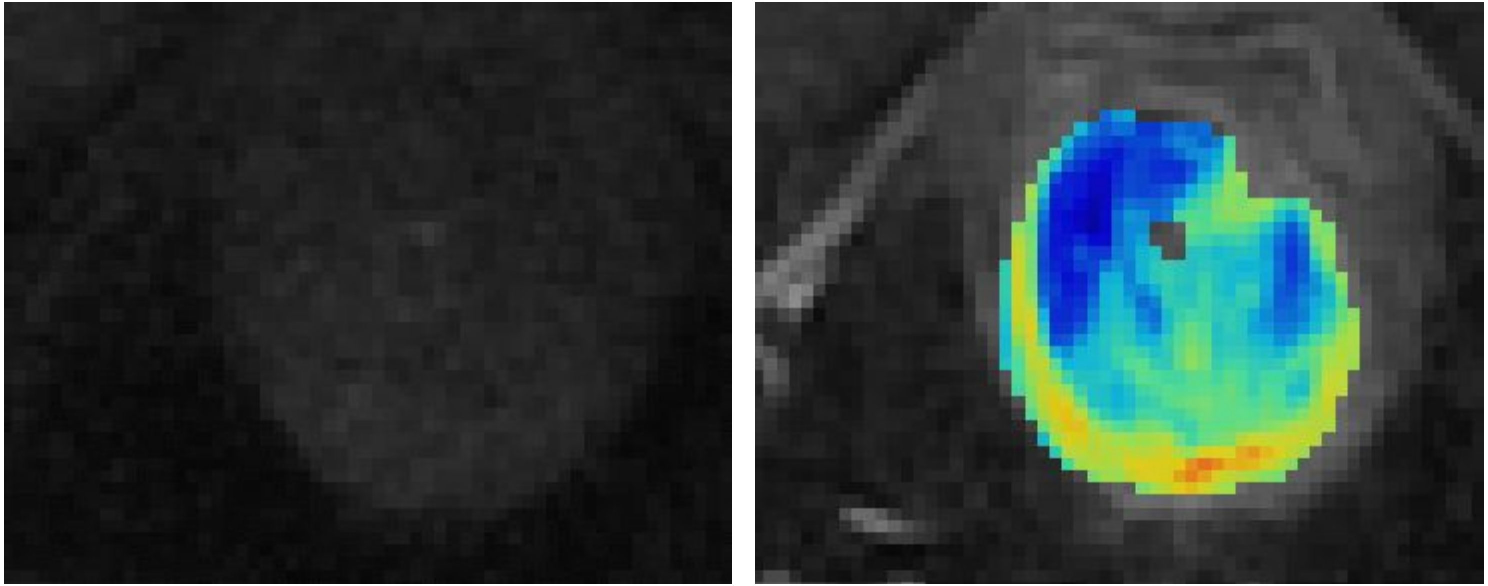


CHANGE IN VARIATION

1. The problem
Dynamic Contrast-Enhanced MRI



- capable monitoring and quantifying perfusion



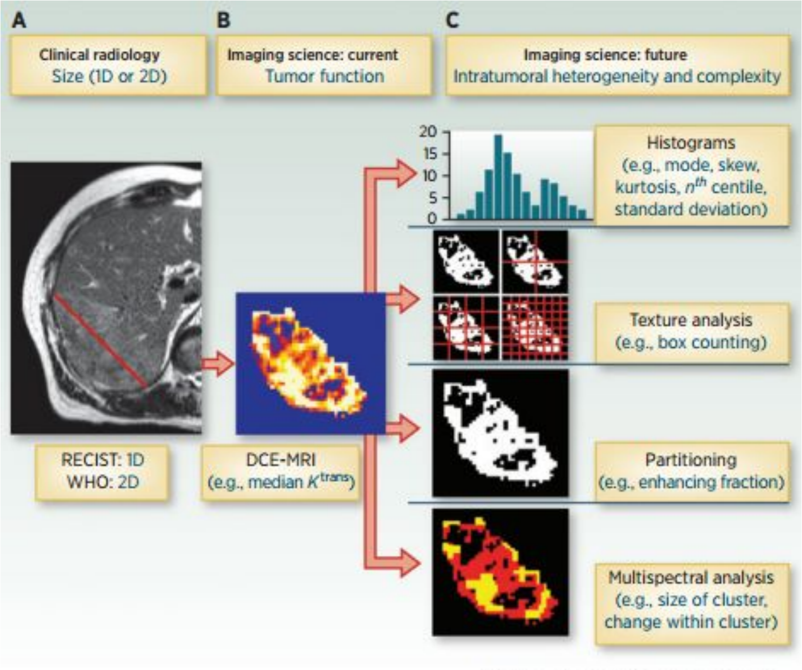
1. The problem
Clinical standards

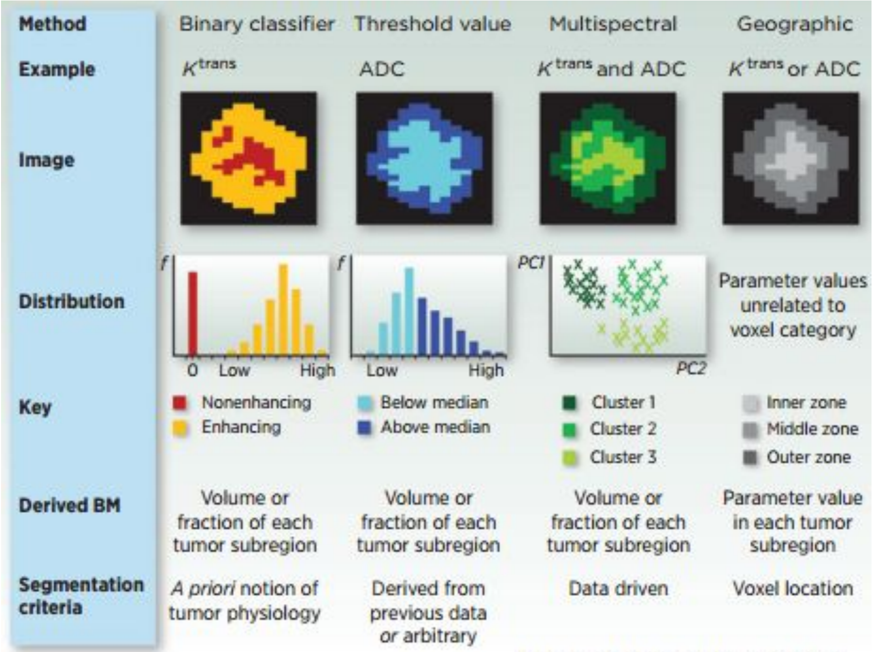
Review

Clinical Cancer Research

Imaging Intratumor Heterogeneity: Role in Therapy Response, Resistance, and Clinical Outcome

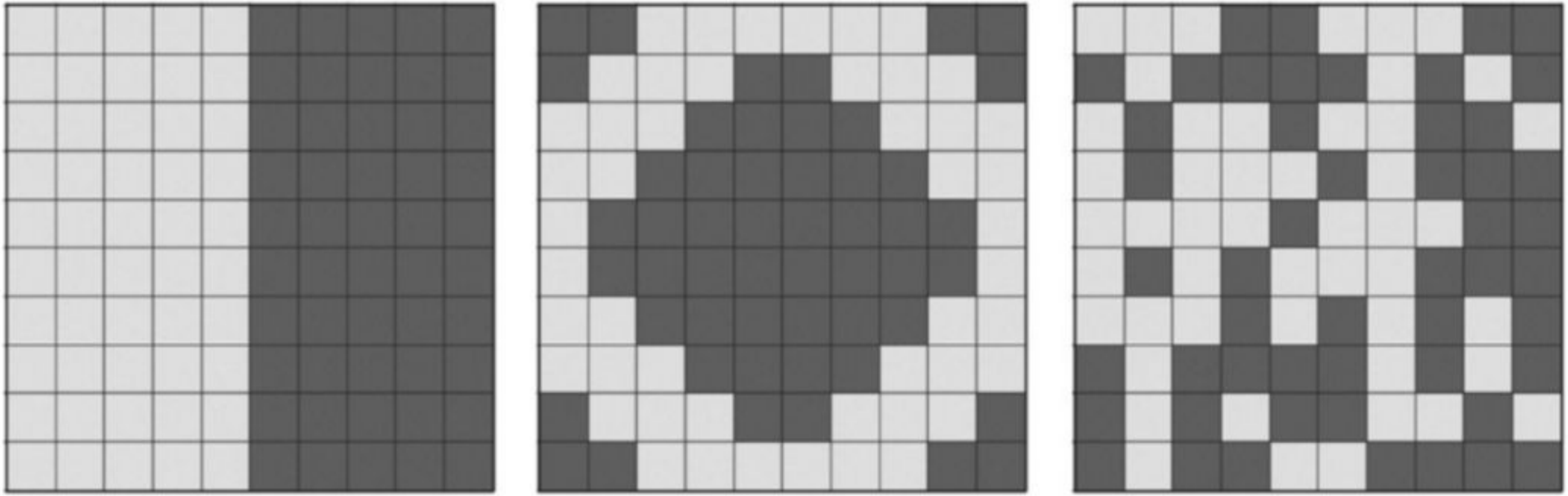
James P.B. O'Connor[1,2], Chris J. Rose[1], John C. Waterton[1,3], Richard A.D. Carano[4], Geoff J.M. Parker[1], and Alan Jackson[1]





1. The problem
Clinical standards

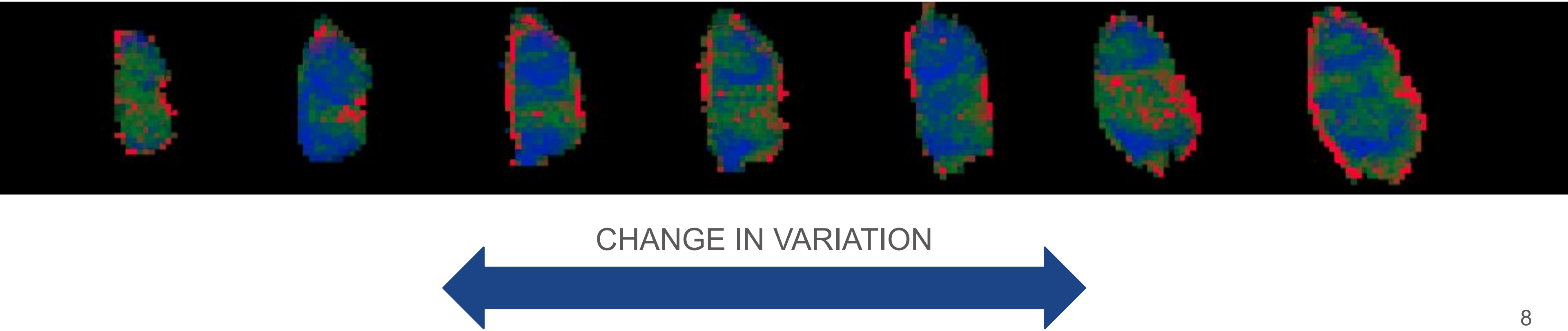
- visual, qualitative or weakly quantitative assessment



2. The question

Q1) Can we characterize tumour growth with the change in its perfusion heterogeneity?

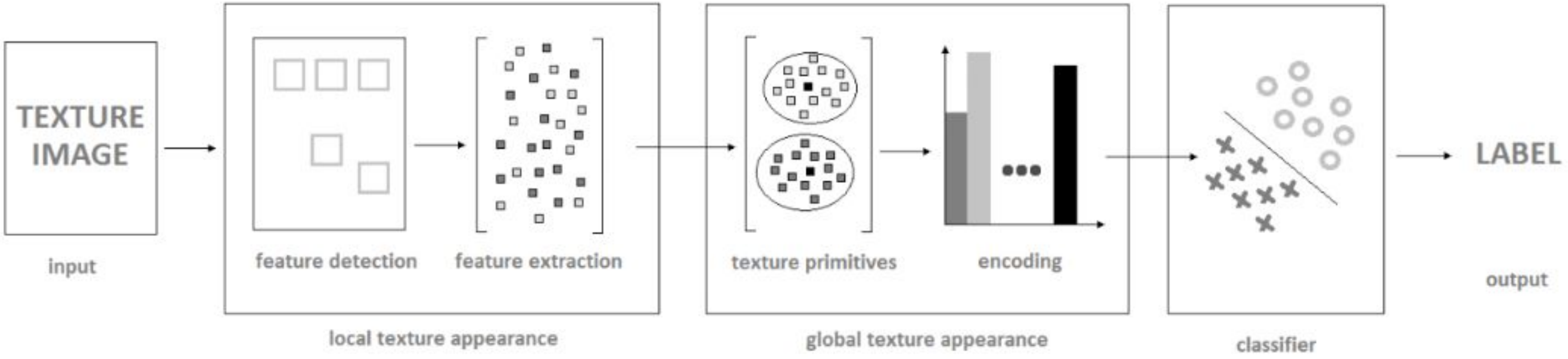
Q2) Can we translate such change into clinical application of therapy assessment and prediction?



3. Trial study: methods

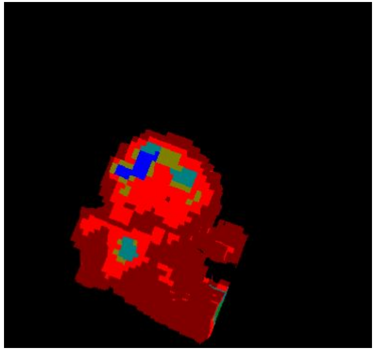
Shallow texture representations

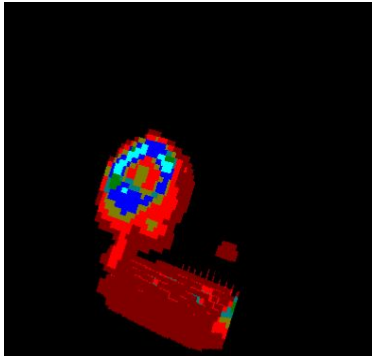
1. allow for training from limited data - **shallow representations**
2. capable of characterizing variation - **texture**
3. some methods robust variation - **patch**

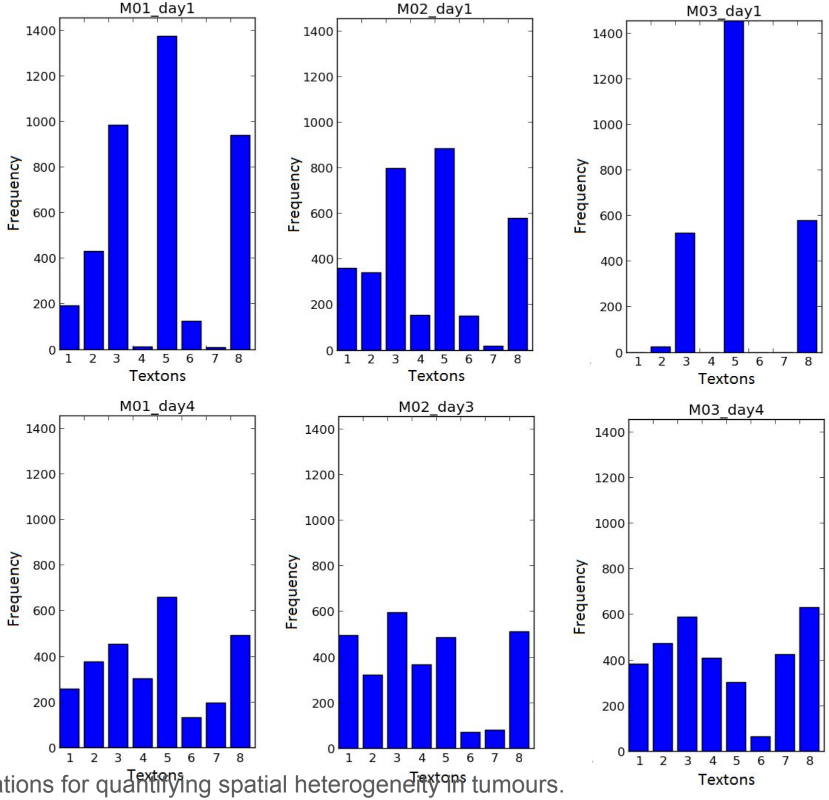


3. Trial study: results

Shallow texture representations



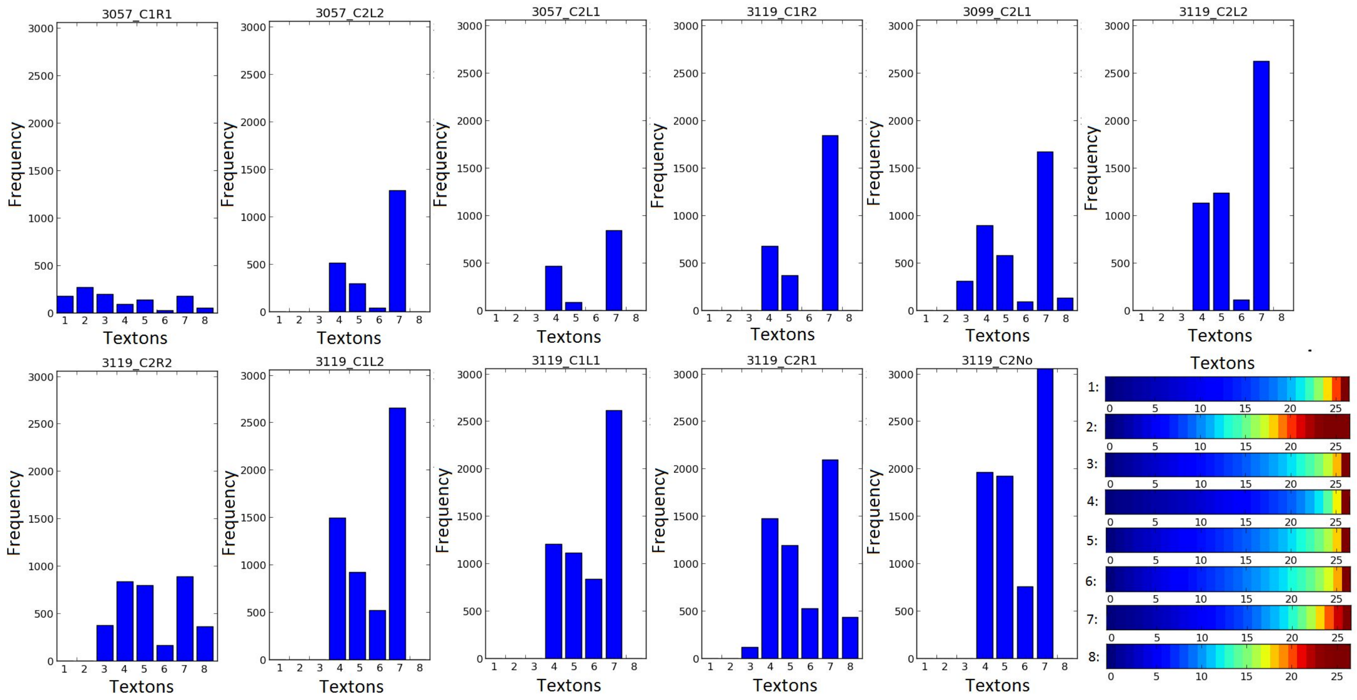




89% acc.
with SVM

3. Trial study: results

Shallow texture representations

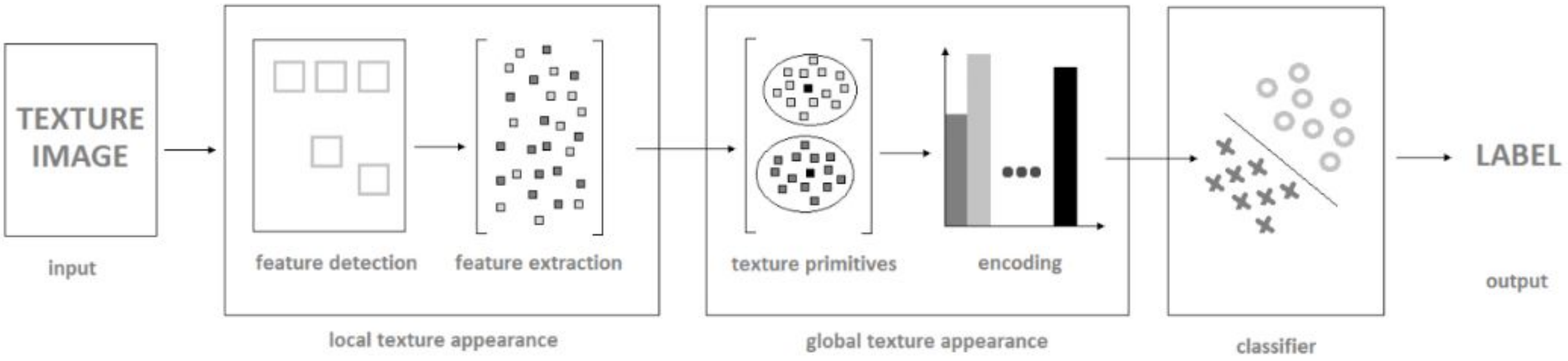


4. Methods

Shallow texture representations

- allow for training from limited data
- capable of characterizing variation

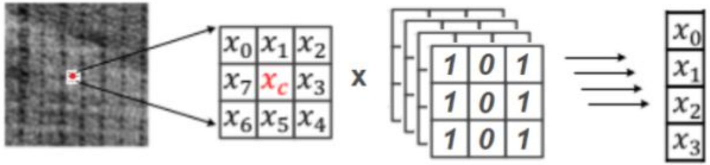
1. **Feature detection:** dense
2. **Feature descriptors:** Voxels, Gabor, Patch, LBP
3. **Visual vocabulary:** KMeans, GMM
4. **Encoding:** BoV
5. **Classifier:** SVM



4. Methods: Gabor

Shallow texture representations

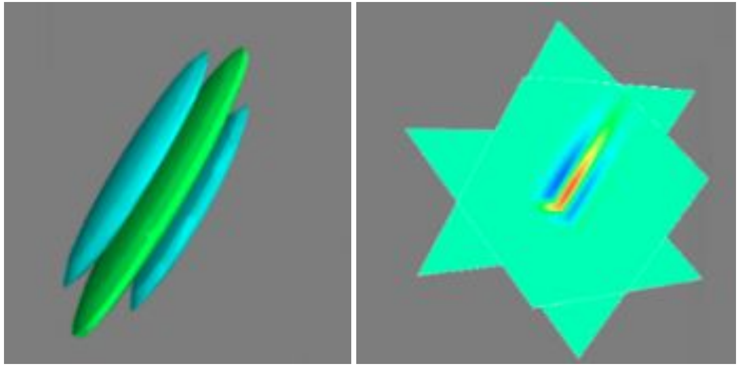
$$\phi_{\theta,\sigma,\gamma,\lambda,\varphi}(x,y) = \exp\left(-\frac{x'^2 + (\gamma y')^2}{2\sigma^2}\right)\cos\left(2\pi\frac{x'}{\lambda} + \varphi\right)$$



$$\phi_{\theta,\sigma,\gamma,\lambda,\varphi}(x,y,z) = \exp\left[-\frac{1}{2}\left(\frac{x'^2}{\sigma_x^2} + \frac{(\gamma y')^2}{\sigma_y^2} + \frac{(\gamma z')^2}{\sigma_z^2}\right)\right]\cos\left(2\pi\frac{x'}{\lambda} + \varphi\right)$$

a) filter bank
feature descriptor

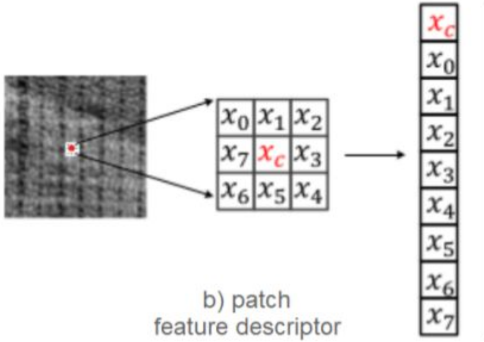
$$\begin{bmatrix} x' \\ y' \\ z' \end{bmatrix} = R(\theta)\begin{bmatrix} x \\ y \\ z \end{bmatrix} \qquad R(\theta) = R_x R_y R_z$$



$$R_x = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta_x & -\sin\theta_x \\ 0 & \sin\theta_x & \cos\theta_x \end{bmatrix} R_y = \begin{bmatrix} \cos\theta_y & 0 & \sin\theta_y \\ 0 & 1 & 0 \\ -\sin\theta_y & 0 & \cos\theta_y \end{bmatrix} R_z = \begin{bmatrix} 0 & \cos\theta_z & -\sin\theta_z \\ 0 & \sin\theta_z & \cos\theta_z \\ 0 & 0 & 1 \end{bmatrix}$$

4. Methods: Patch

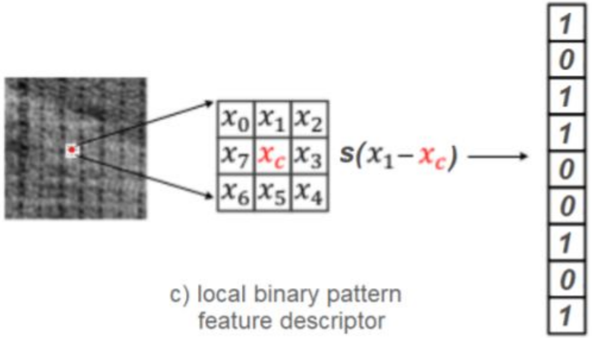
Shallow texture representations



4. Methods: LBP

Shallow texture representations

$$LBP(i,j,k) = \sum_{p=-n/2}^{n/2} \sum_{r=-n/2}^{n/2} \sum_{s=-n/2}^{n/2} s(I(i-p,j-r,k-s) - I(i,j,k))2^{prs}$$



c) local binary pattern feature descriptor

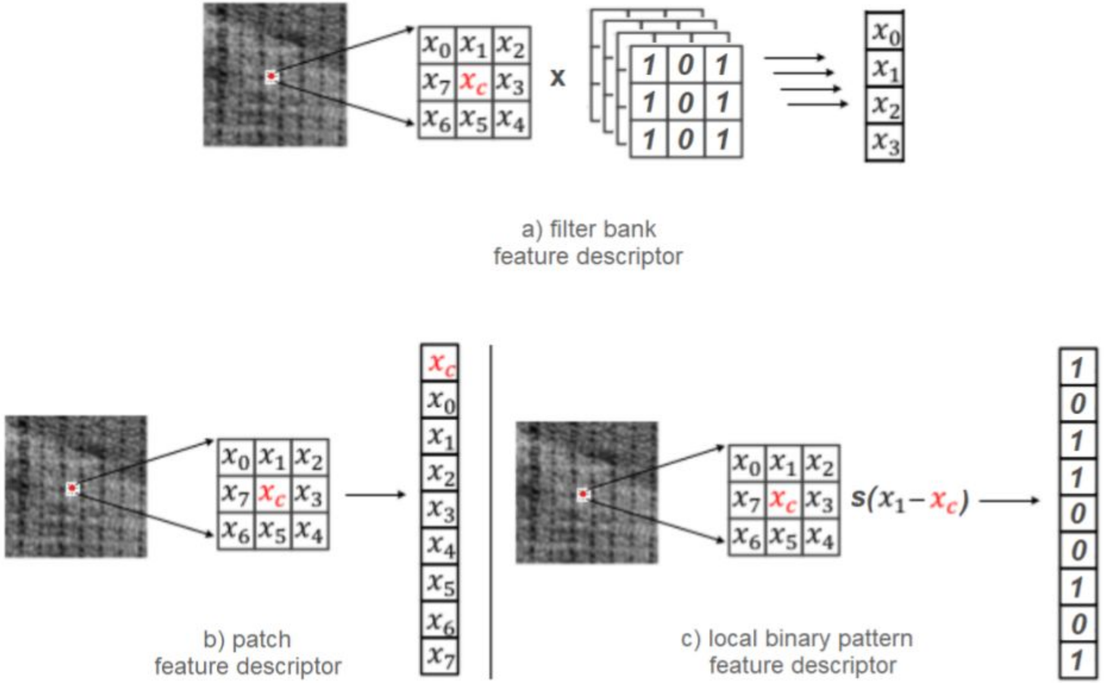
$$s(x) = \begin{cases} 1 & x \geq 0 \\ 0 & x < 0 \end{cases}$$

$$\text{ELBP\_CI}_p(x_c) = s(x_c - \beta)$$

$$\text{ELBP\_NI}_p(x_c) = \sum_{i=1}^{n^3} s(x_i - \beta_p)2^i$$

4. Methods: feature descriptors

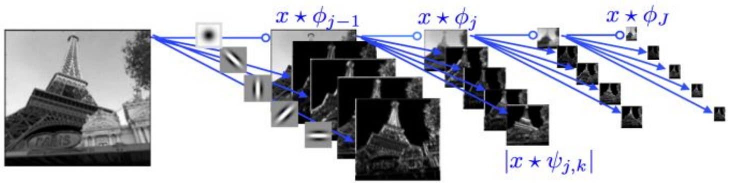
Shallow texture representations

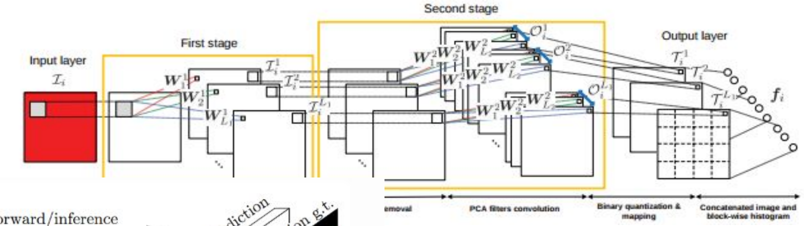


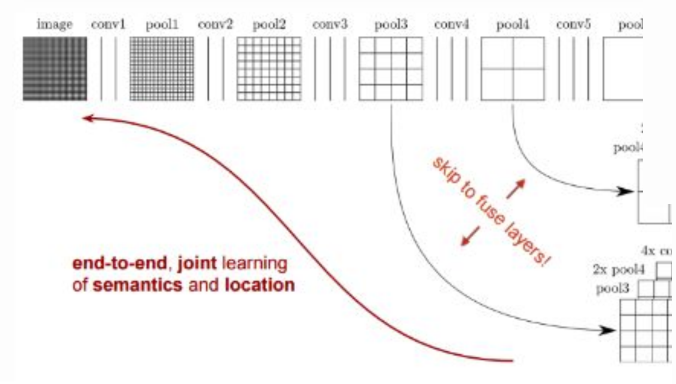
4. Methods

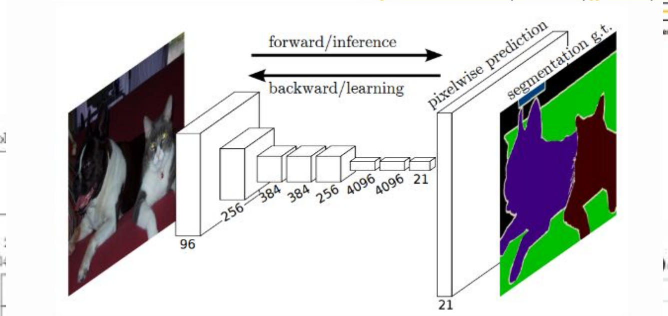
Deep texture representations

- allow for training from limited data
- capable of characterizing variation









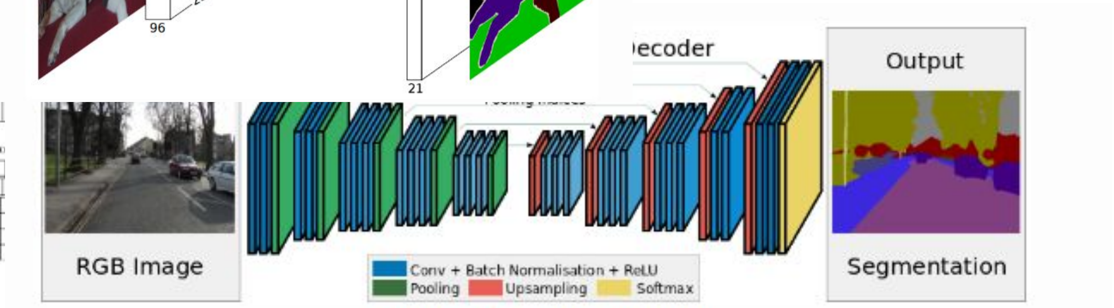


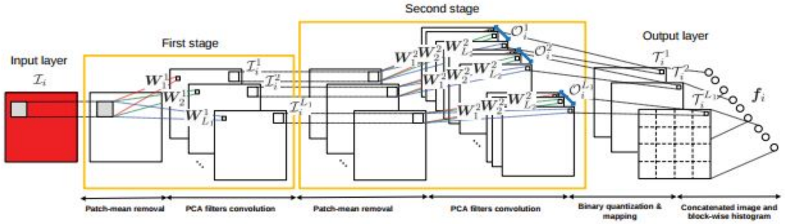
Figure : The SegNet Architecture

4. Methods
Deep texture representations

1. **transfer learning:** feature extractor
2. **hand-crafted nets:** random projections

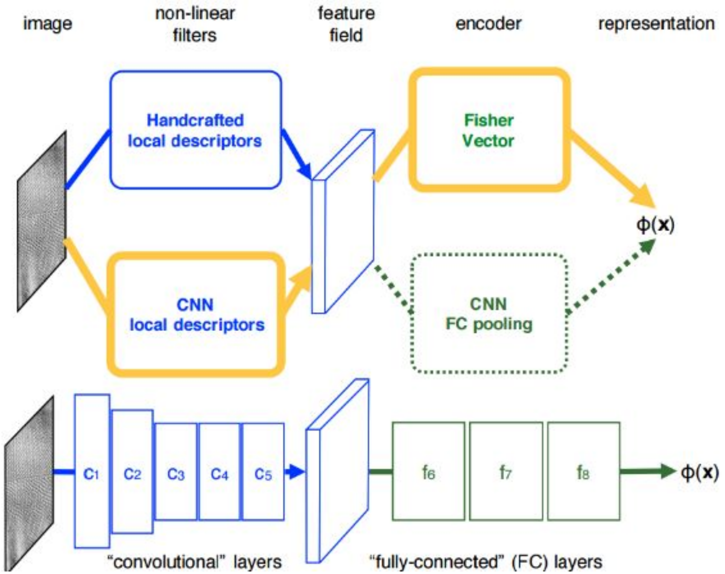
PCANet: A Simple Deep Learning Baseline for Image Classification?

Tsung-Han Chan, Kui Jia, Shenghua Gao, Jiwen Lu, Zinan Zeng, and Yi Ma



Deep Filter Banks for Texture Recognition and Segmentation

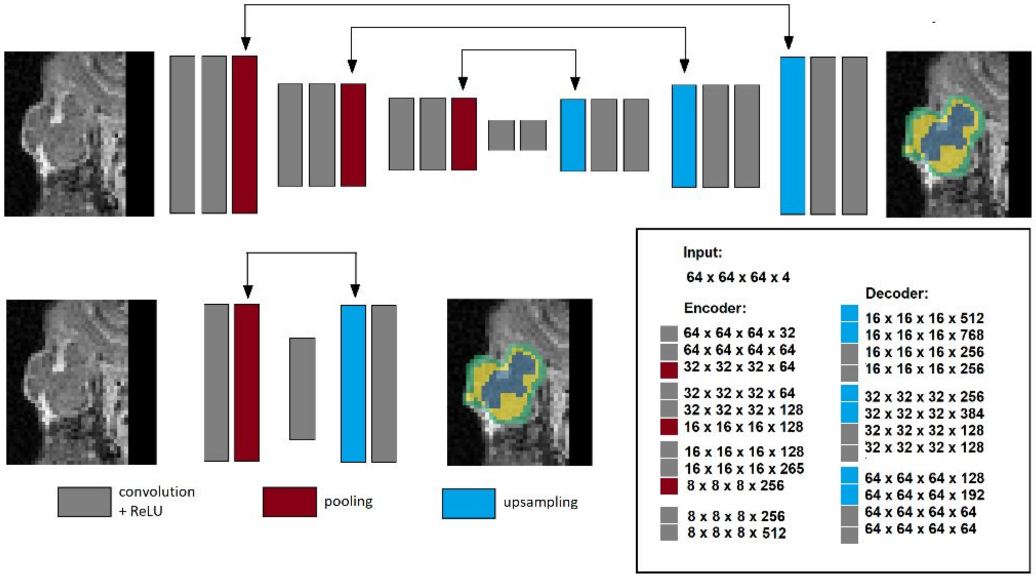
Mircea Cimpoi, University of Oxford; Subhransu Maji, University of Massachusetts, Amherst; Andrea Vedaldi, University of Oxford

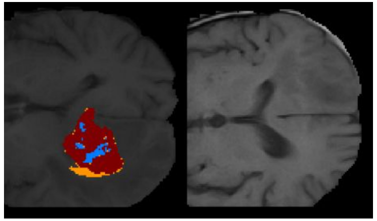


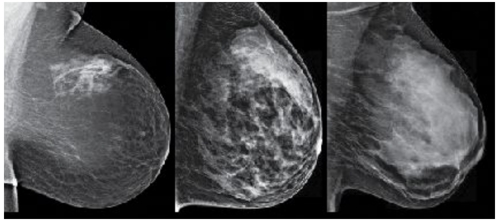
4. Methods
Deep texture representations

T-UNet

Rand-UNet

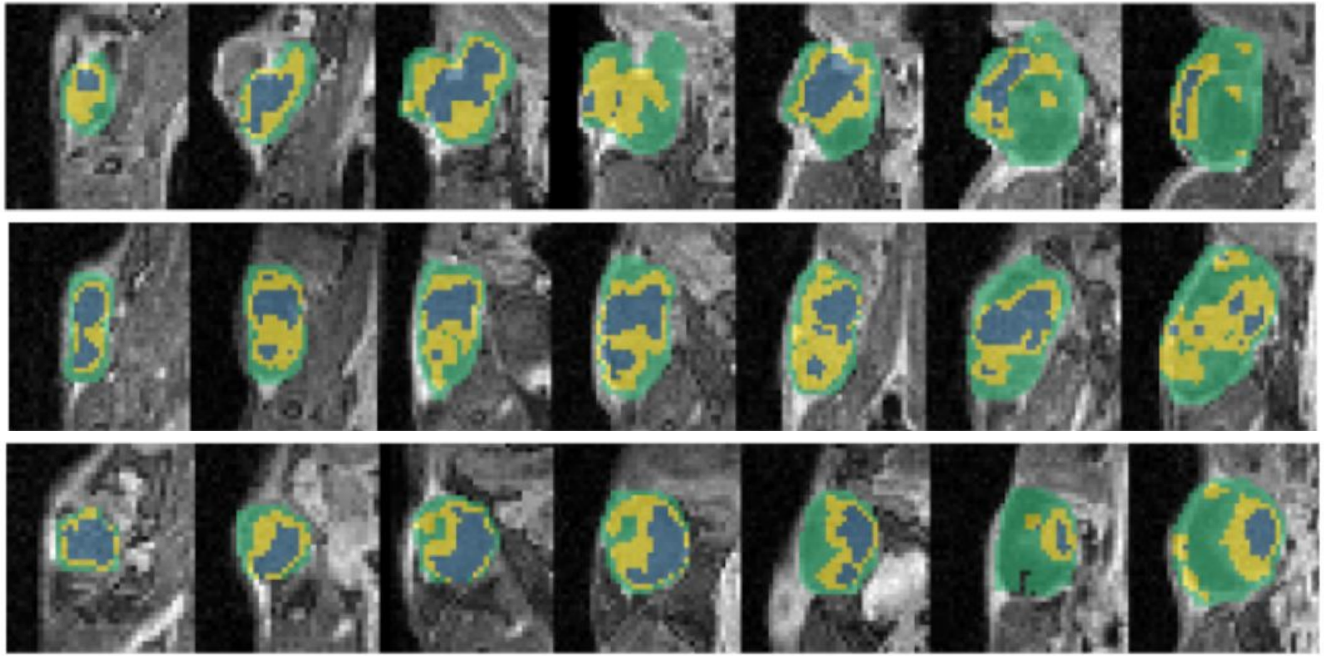


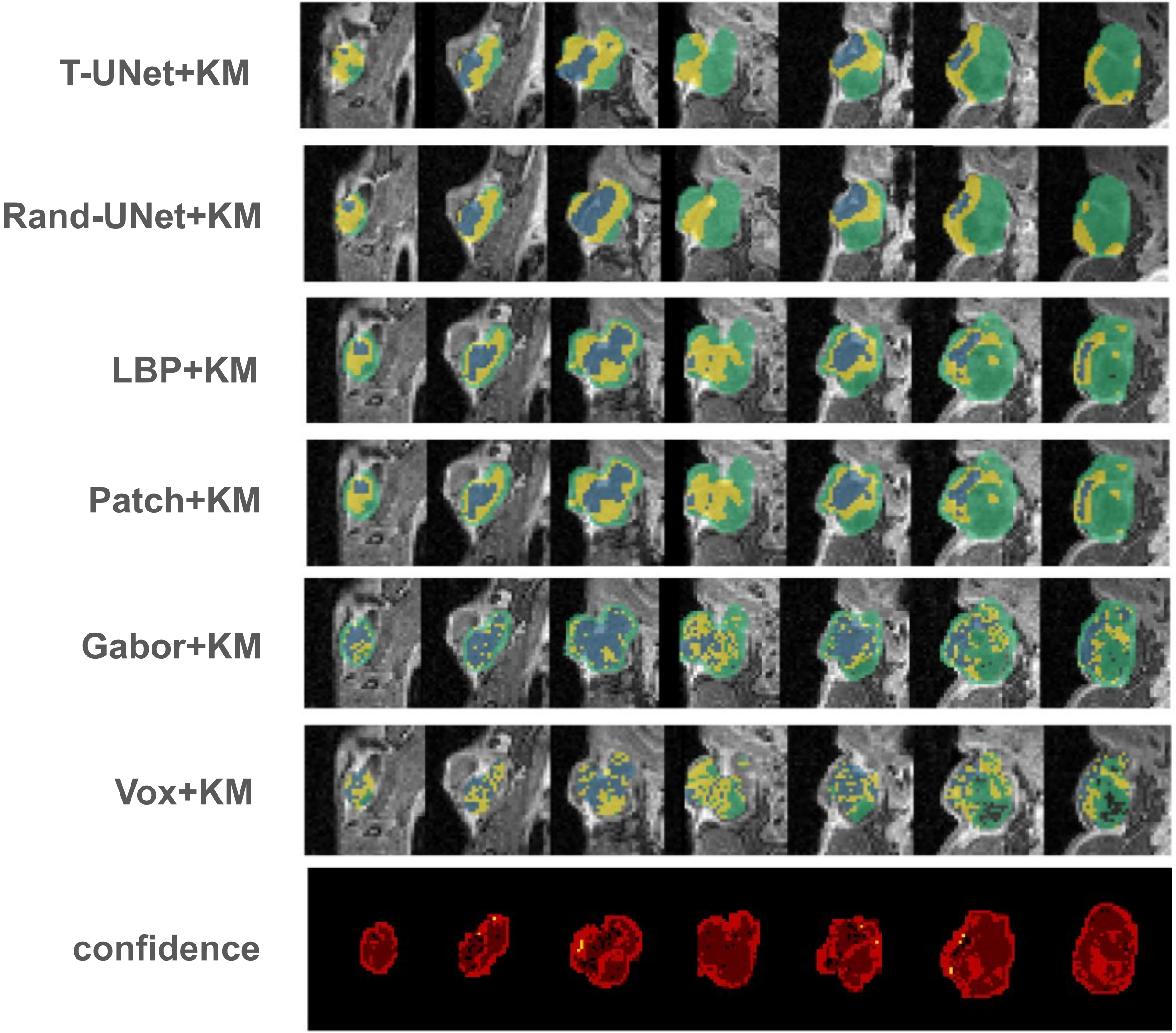




5. Results: segmentations

Pre-clinical: tumour progression




T-UNet+KM
Rand-UNet+KM
LBP+KM
Patch+KM
Gabor+KM
Vox+KM
confidence

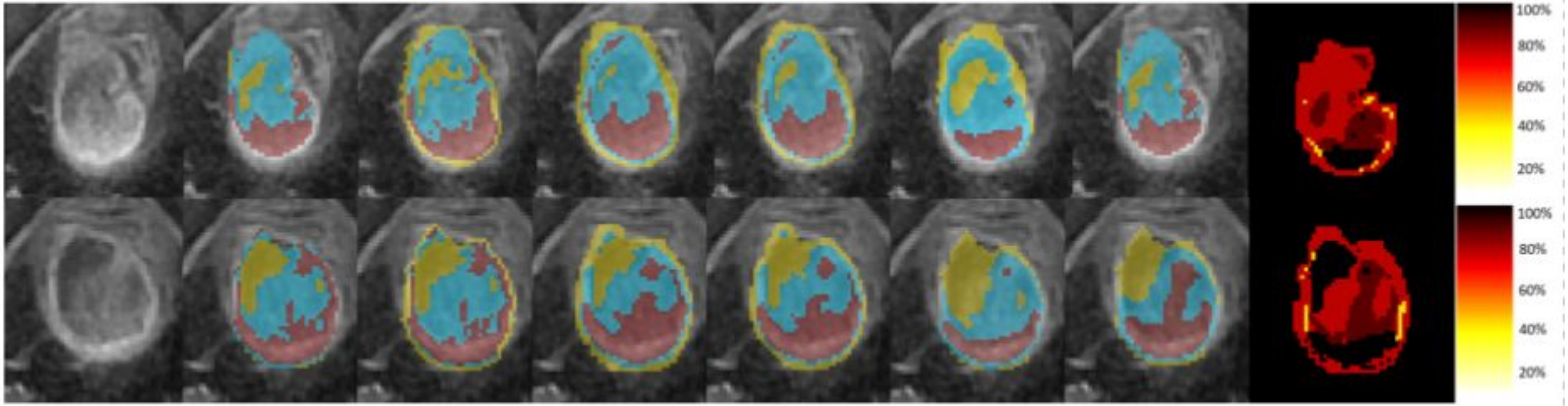
5. Results: classifications

Pre-clinical: tumour progression

	Vox	Filters	Patch	LBP	UNet	RandUNet
	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE
KM	65% | 0.599	70% | 0.604	70% | 0.715	**75% | 0.723**	**80% | 0.825**	**75% | 0.729**
GMM	**82.5%** | 0.516	70% | 0.754	**70% | 0.958**	**70% | 0.963**	**77.5% | 0.783**	**75% | 0.715**

5. Results: segmentations

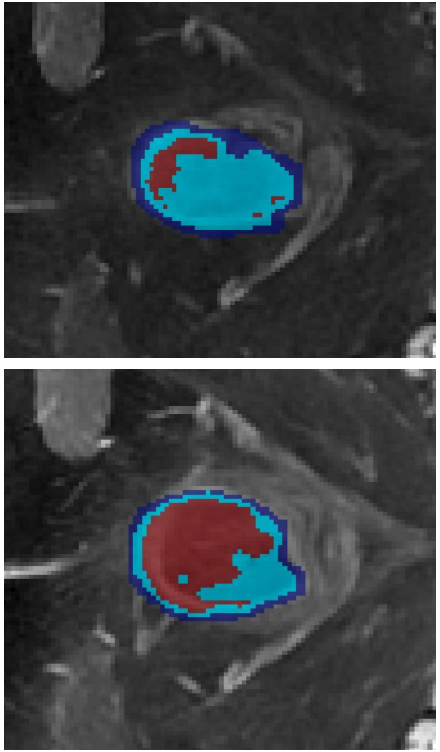
Clinical: therapy response

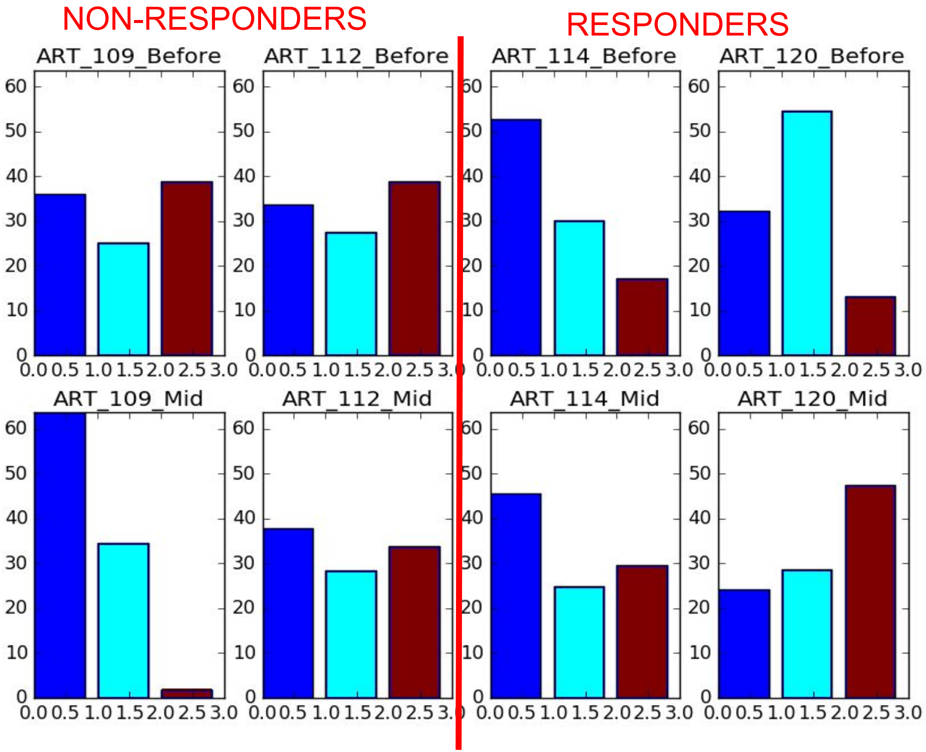


5. Results: classifications

Clinical: therapy response

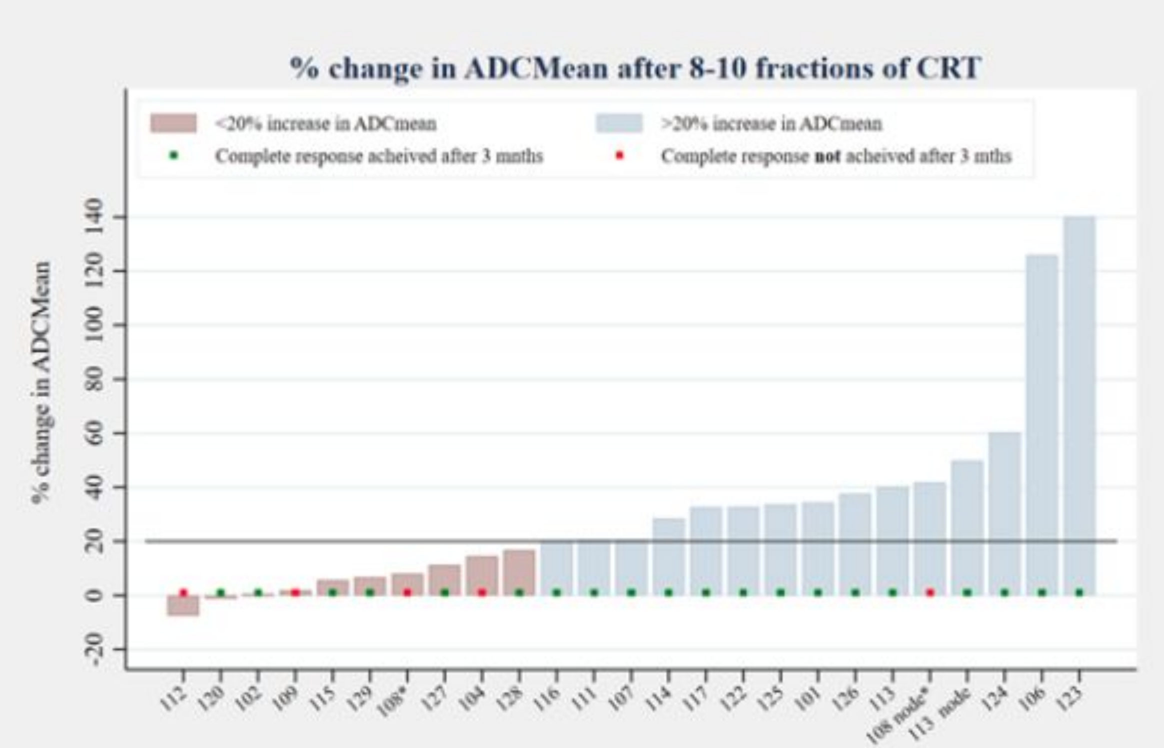
$$J\_SAD = \sum_{j=1}^{6} \sum_{i=0}^{k} abs(h_{j,1}(i) - h_{j,2}(i))$$





Part 1: Results

Question 2: Clinical application - therapy assessment



25

Quantifying Spatial Perfusion Heterogeneity in Tumours from DCE-MRI

Jola Mirecka

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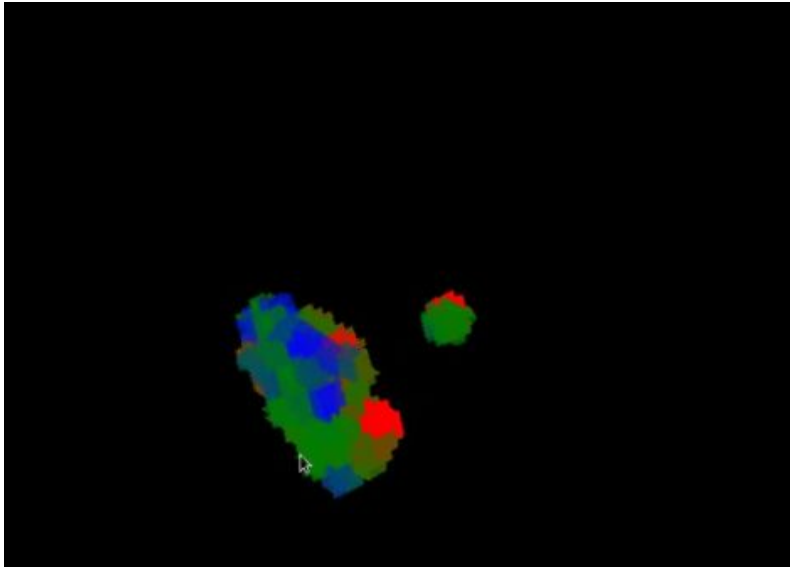

- ★ Collaborators: **Bartek Papiez, Benjamin Irving**
- ★ Pre-clinical collaborators: **Pavitra Kannan, Ana Gomes, Veerle Kesermans, Danny Allen, Paul Kinchesh, Sean Smart**
- ★ Clinical collaborators: **Ben George, Maria Hawkins**
- ★ Supervisors: **Mark Jenkinson, Julia Schnabel** and **Michael Chappell, Mike Brady** (advisory)

Questions?

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EPSRC

Cryo-EM?

- structure to function
- resolution revolution
- pharmaceutical implications

eBIC facilities

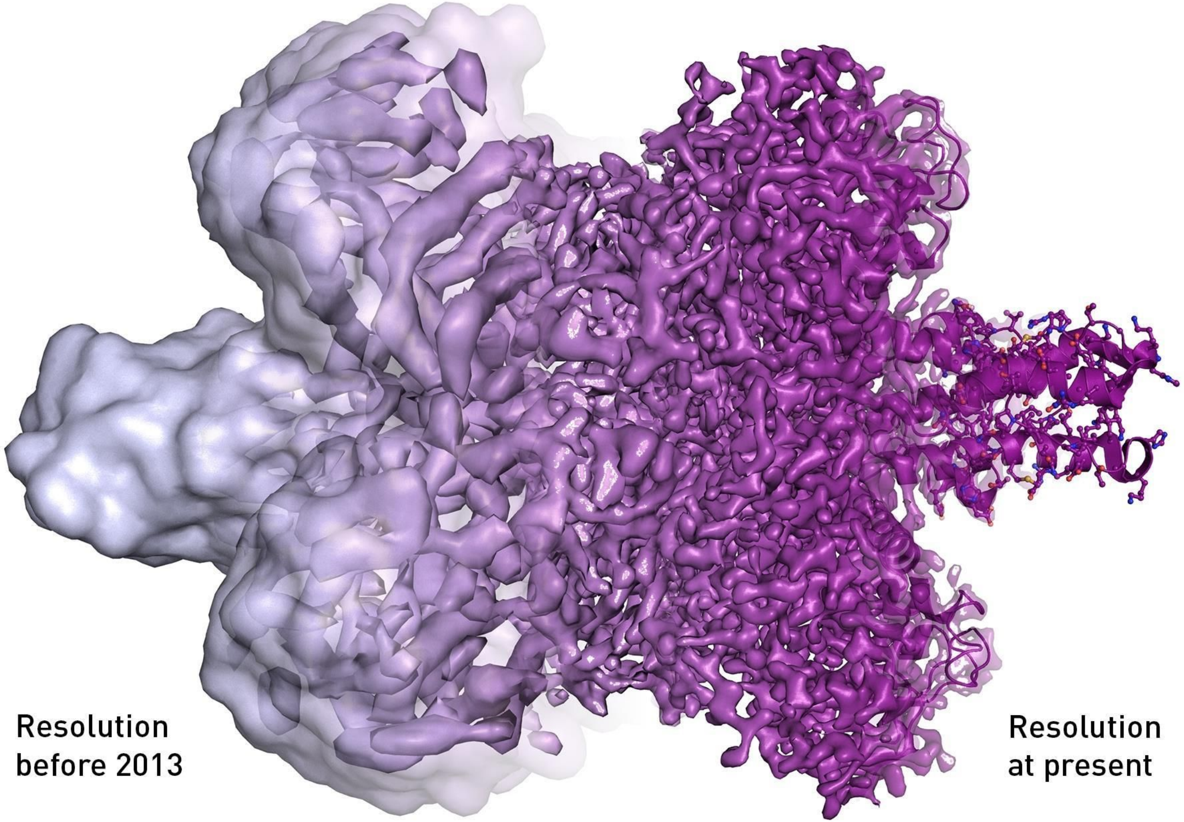
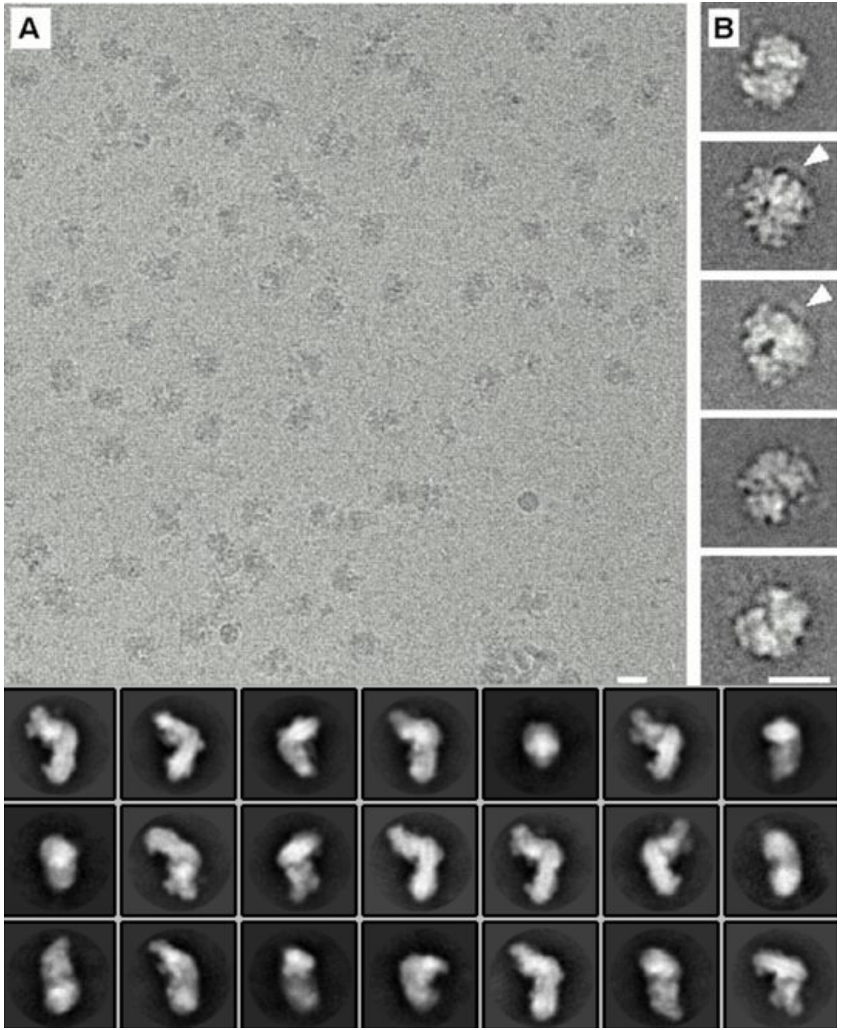


Illustration: ©Martin Högbom/The Royal Swedish Academy of Sciences

Cryo-EM?

Particle picking:

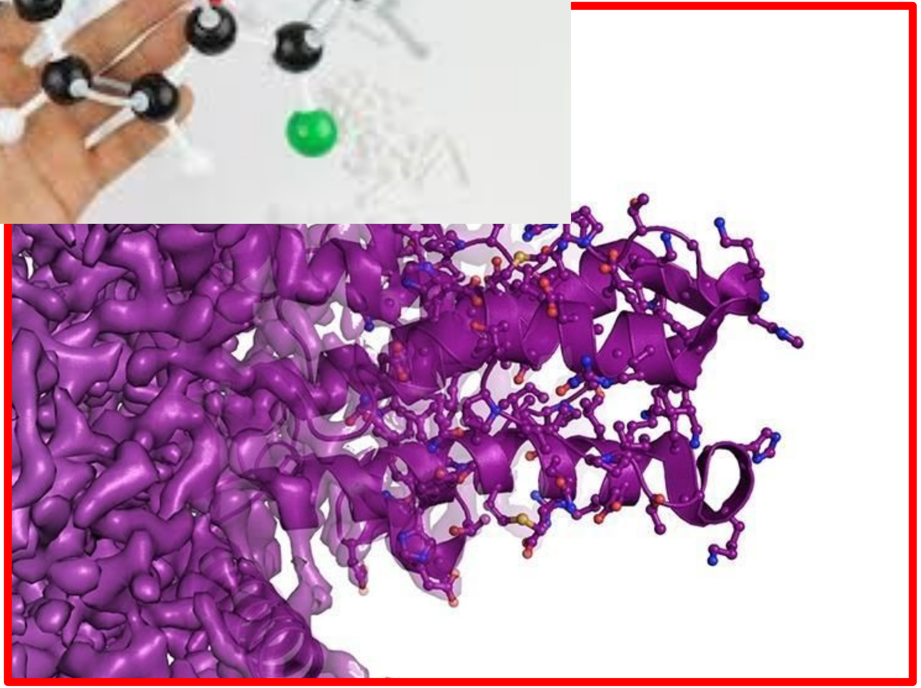
- noisy micrographs
- picking particles
- 2D classification



Cryo-EM?

Model building:

- density segmentation
- secondary structure
- side chains

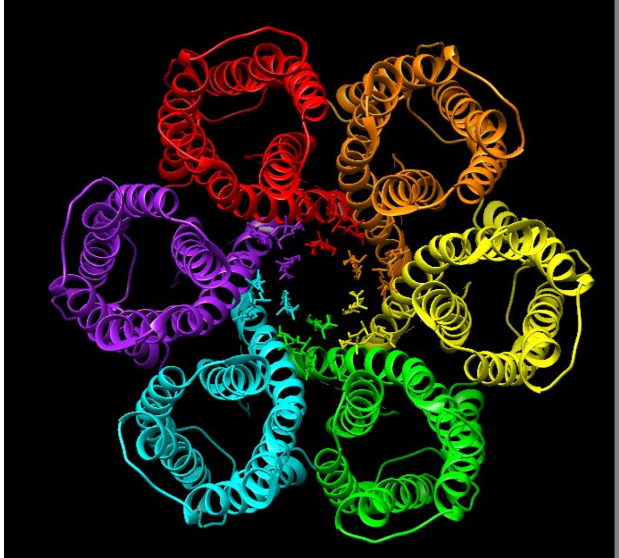


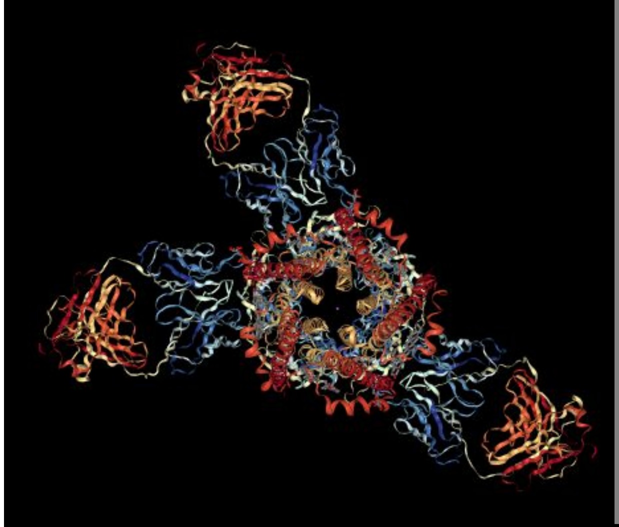
Cryo-EM?

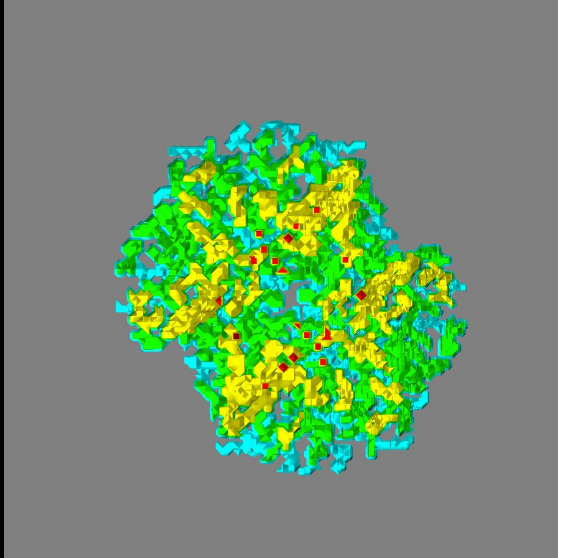
Model building:

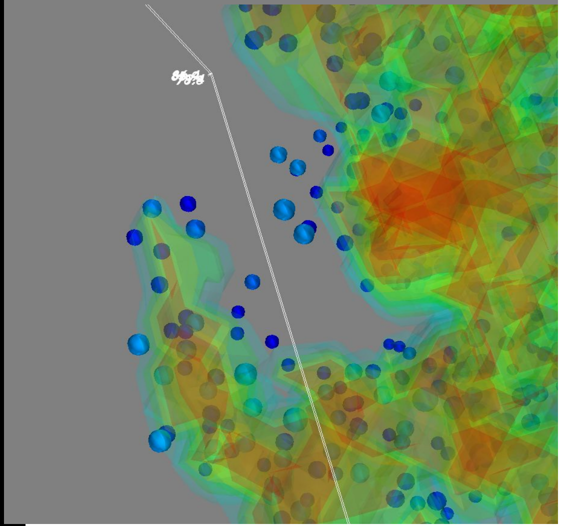
- density segmentation
- secondary structure
- side chains

Ribosome: 100 000 atoms





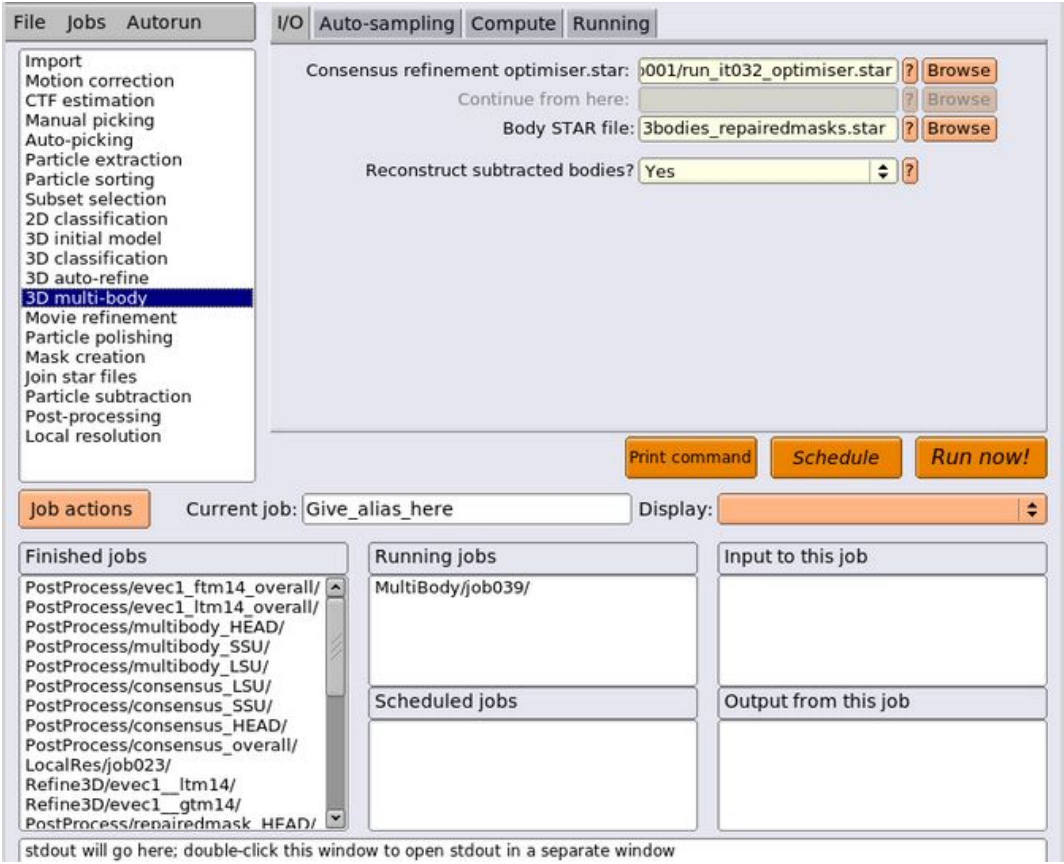




Cryo-EM?

Pipeline automation:

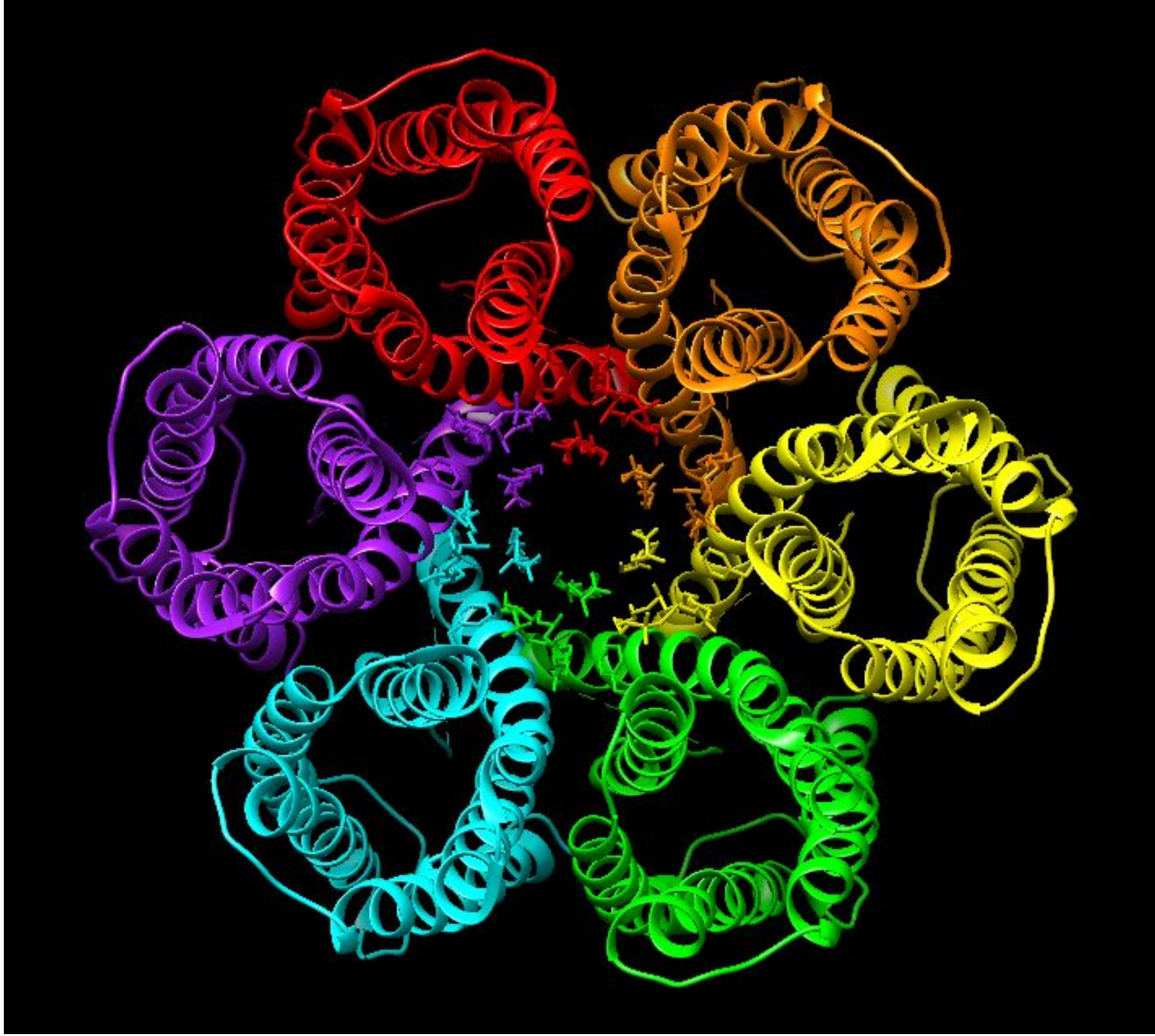
- automatic parameter selection
- data model



Questions?

CCP-EM:
Tom Burnley
Colin Palmer
Agnel Joseph
Martyn Winn

SciML:
Tony Hey
Jeyan Thiyagalingam



Presentation outline

1. **The problem**

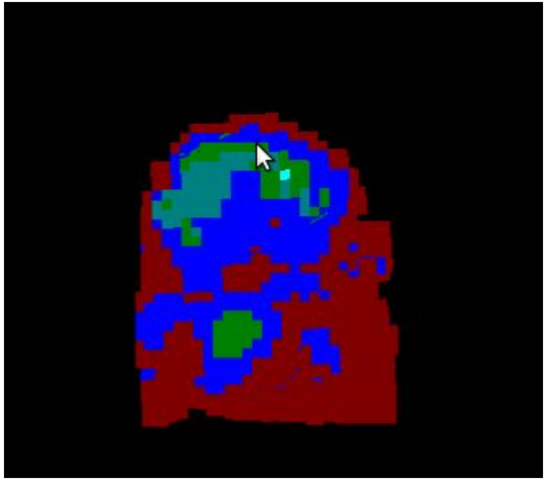
2. **The question**

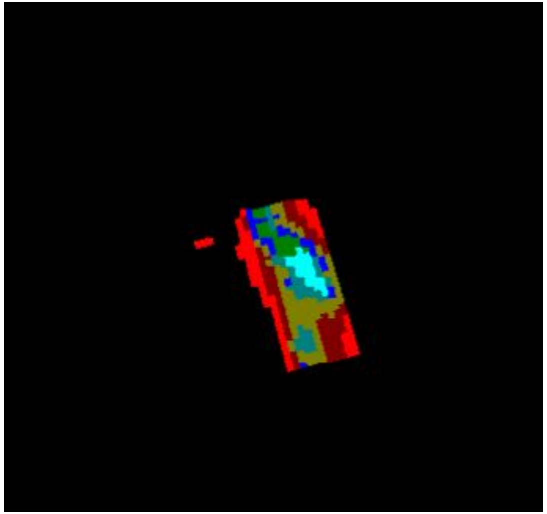
3. **Trial study:**
   3.1. shallow image representations

4. **Methods**:
   4.1. shallow image representations
   4.2. deep image representations

5. **Results**:
   5.1. pre-clinical: tumour progression
   5.2. clinical: response to therapy

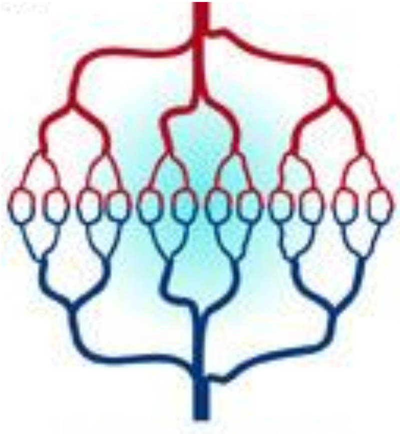
6. **Cryo-EM?**



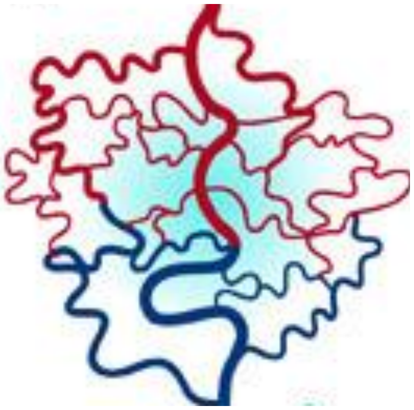


1. The problem
Tumours and heterogeneity

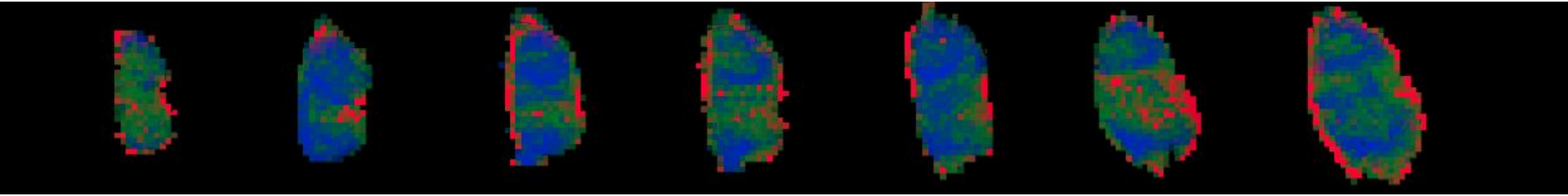
- cancerous tumours are characterized by an increase in heterogeneity
  - ✶ heterogeneity - variation or non-uniformity in composition



normal vasculature

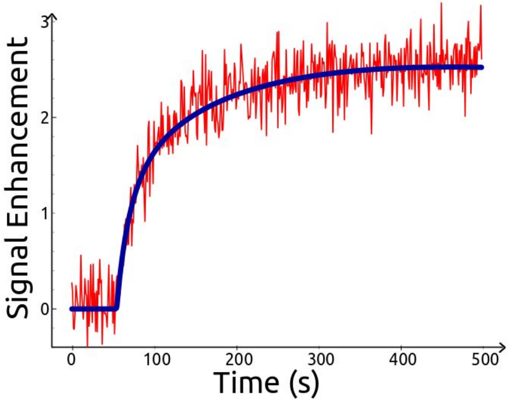


tumour vasculature

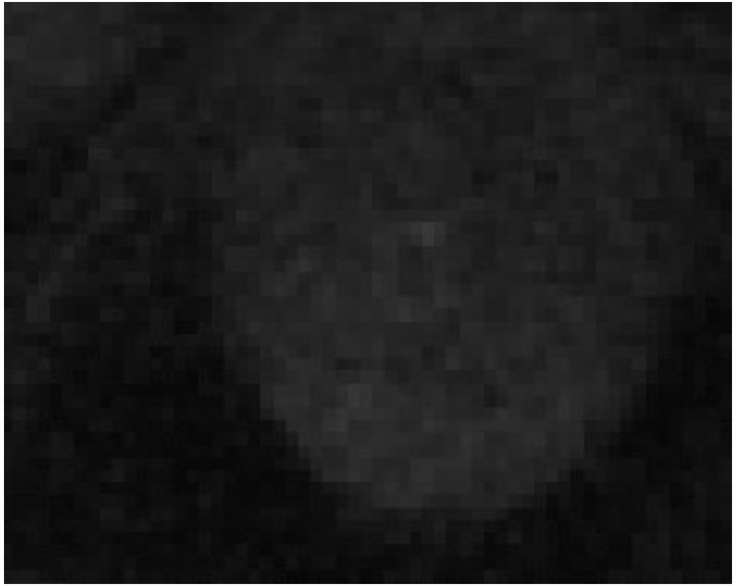


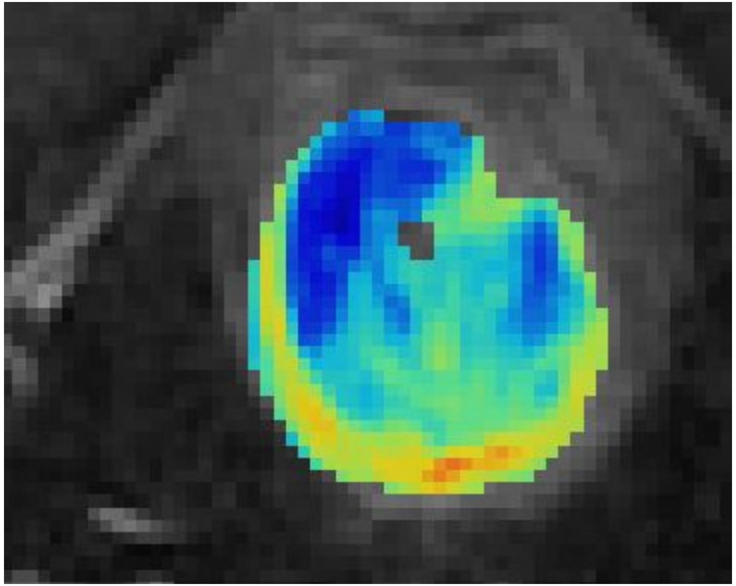
CHANGE IN VARIATION

1. The problem
Dynamic Contrast-Enhanced MRI



- capable monitoring and quantifying perfusion





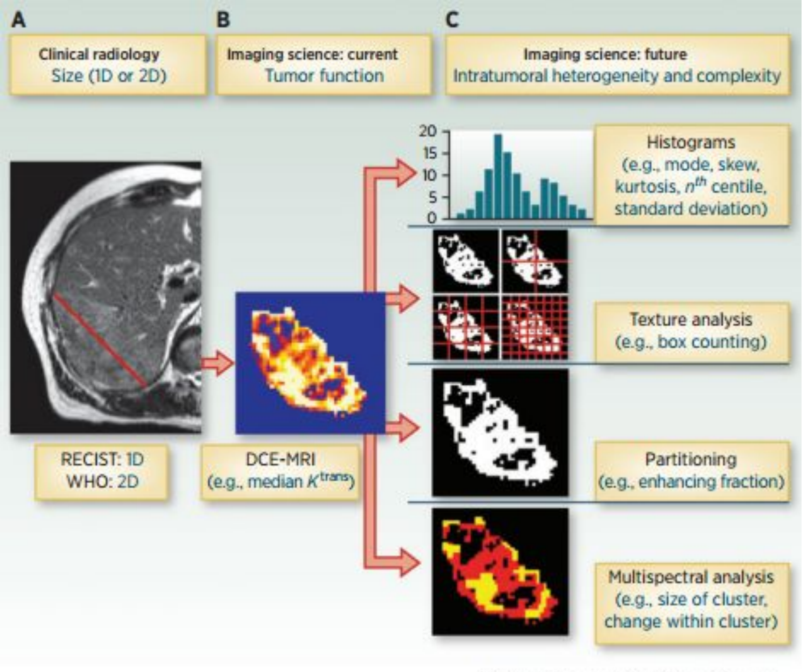
1. The problem
Clinical standards

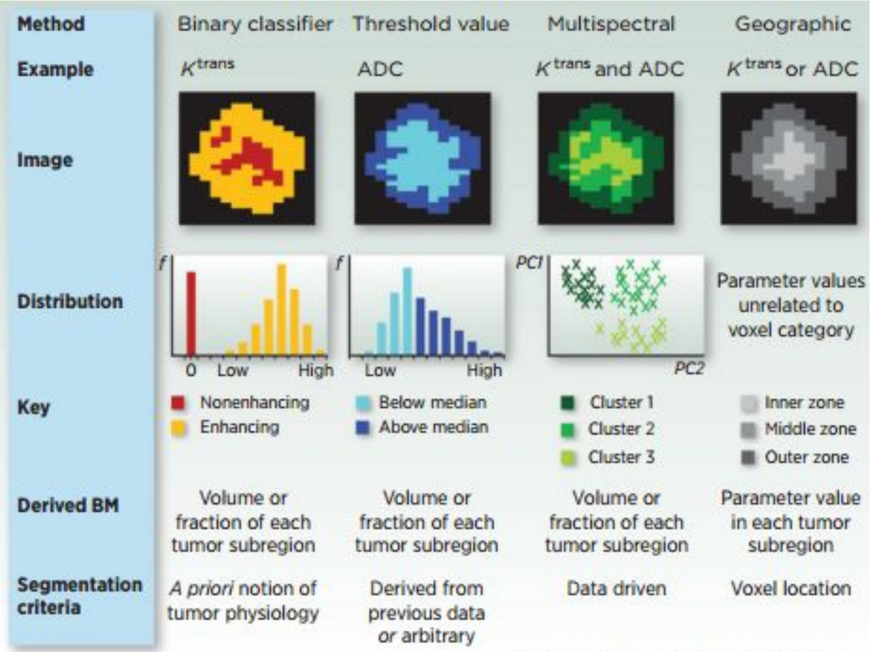
Review

Clinical Cancer Research

Imaging Intratumor Heterogeneity: Role in Therapy Response, Resistance, and Clinical Outcome

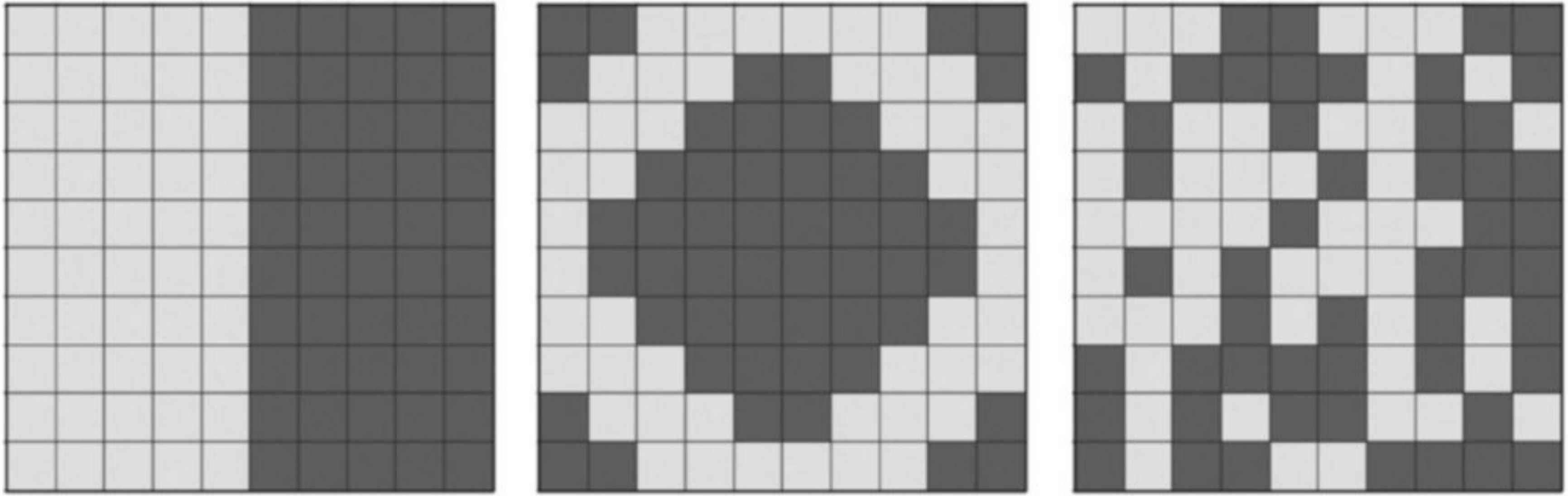
James P.B. O'Connor[1,2], Chris J. Rose[1], John C. Waterton[1,3], Richard A.D. Carano[4], Geoff J.M. Parker[1], and Alan Jackson[1]





1. The problem
Clinical standards

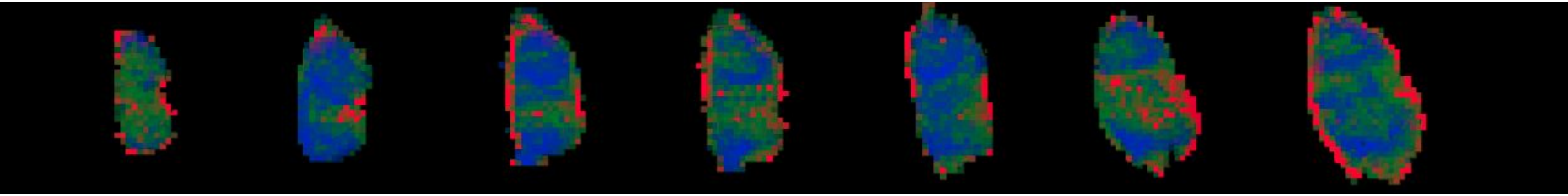
- visual, qualitative or weakly quantitative assessment



2. The question

Q1) Can we characterize tumour growth with the change in its perfusion heterogeneity?

Q2) Can we translate such change into clinical application of therapy assessment and prediction?

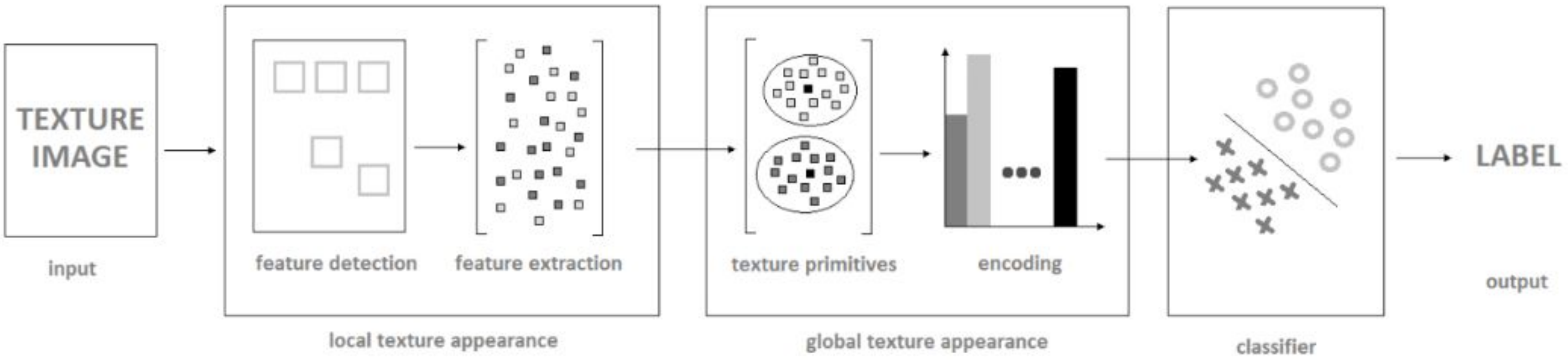


CHANGE IN VARIATION

3. Trial study: methods

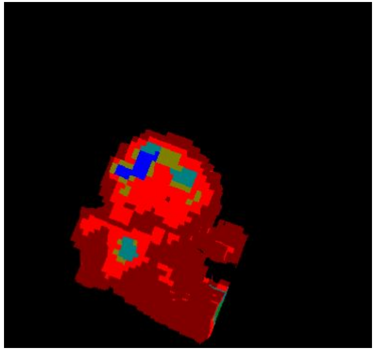
Shallow texture representations

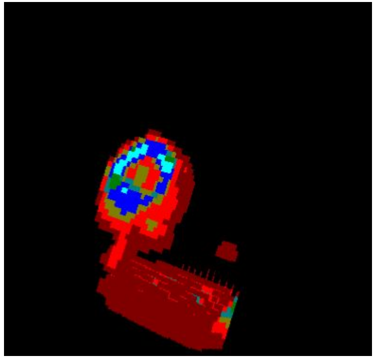
1. allow for training from limited data - **shallow representations**
2. capable of characterizing variation - **texture**
3. some methods robust variation - **patch**

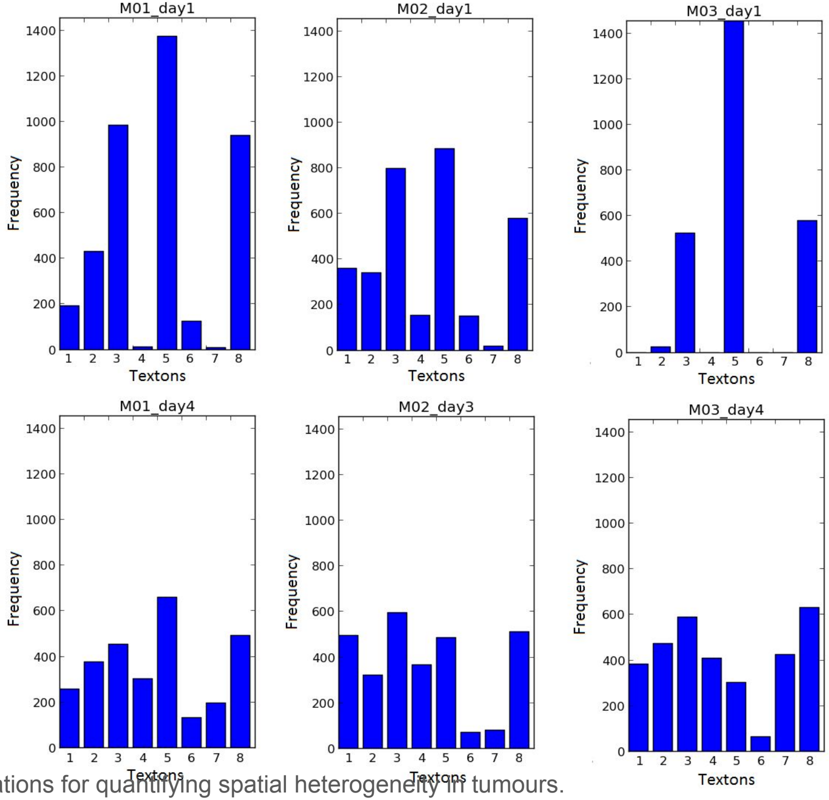


3. Trial study: results

Shallow texture representations

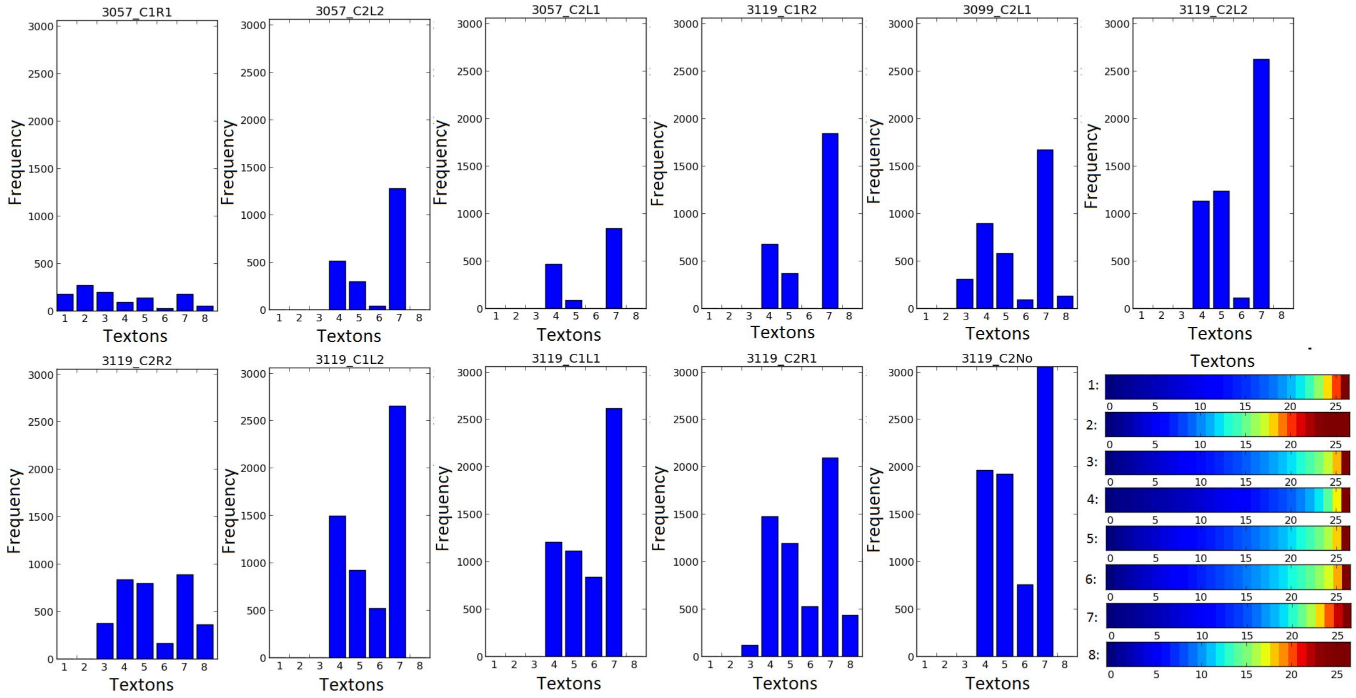






89% acc. with SVM

3. Trial study: results
Shallow texture representations

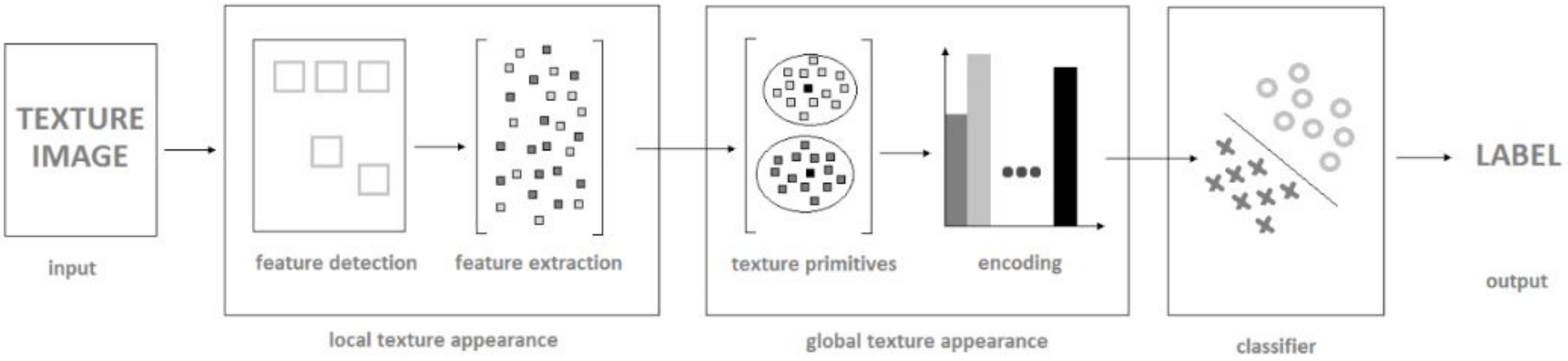


4. Methods

Shallow texture representations

- allow for training from limited data
- capable of characterizing variation

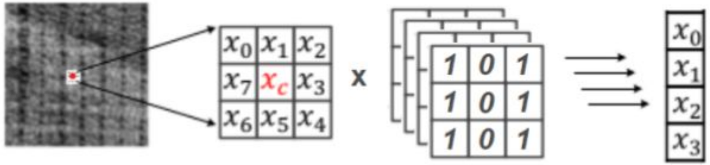
1. **Feature detection:** dense
2. **Feature descriptors:** Voxels, Gabor, Patch, LBP
3. **Visual vocabulary:** KMeans, GMM
4. **Encoding:** BoV
5. **Classifier:** SVM



4. Methods: Gabor

Shallow texture representations

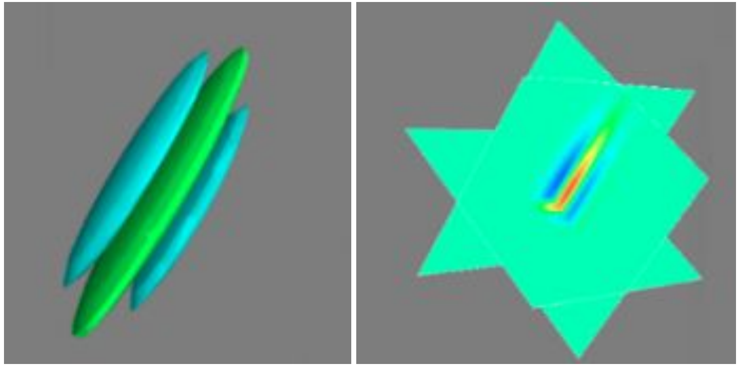
$$\phi_{\theta,\sigma,\gamma,\lambda,\varphi}(x,y) = \exp\left(-\frac{x'^2 + (\gamma y')^2}{2\sigma^2}\right)\cos\left(2\pi\frac{x'}{\lambda}+\varphi\right)$$



a) filter bank
feature descriptor

$$\phi_{\theta,\sigma,\gamma,\lambda,\varphi}(x,y,z) = \exp\left[-\frac{1}{2}\left(\frac{x'^2}{\sigma_x^2} + \frac{(\gamma y')^2}{\sigma_y^2} + \frac{(\gamma z')^2}{\sigma_z^2}\right)\right]\cos\left(2\pi\frac{x'}{\lambda}+\varphi\right)$$

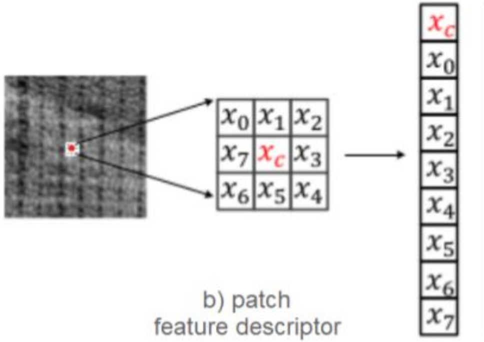
$$\begin{bmatrix} x' \\ y' \\ z' \end{bmatrix} = R(\theta)\begin{bmatrix} x \\ y \\ z \end{bmatrix} \qquad R(\theta) = R_x R_y R_z$$



$$R_x = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\theta_x & -\sin\theta_x \\ 0 & \sin\theta_x & \cos\theta_x \end{bmatrix} R_y = \begin{bmatrix} \cos\theta_y & 0 & \sin\theta_y \\ 0 & 1 & 0 \\ -\sin\theta_y & 0 & \cos\theta_y \end{bmatrix} R_z = \begin{bmatrix} 0 & \cos\theta_z & -\sin\theta_z \\ 0 & \sin\theta_z & \cos\theta_z \\ 0 & 0 & 1 \end{bmatrix}$$

4. Methods: Patch

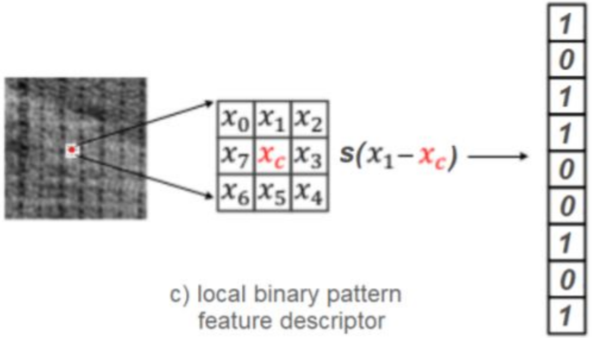
Shallow texture representations



4. Methods: LBP

Shallow texture representations

$$LBP(i,j,k) = \sum_{p=-n/2}^{n/2} \sum_{r=-n/2}^{n/2} \sum_{s=-n/2}^{n/2} s(I(i-p, j-r, k-s) - I(i,j,k))2^{prs}$$



c) local binary pattern feature descriptor

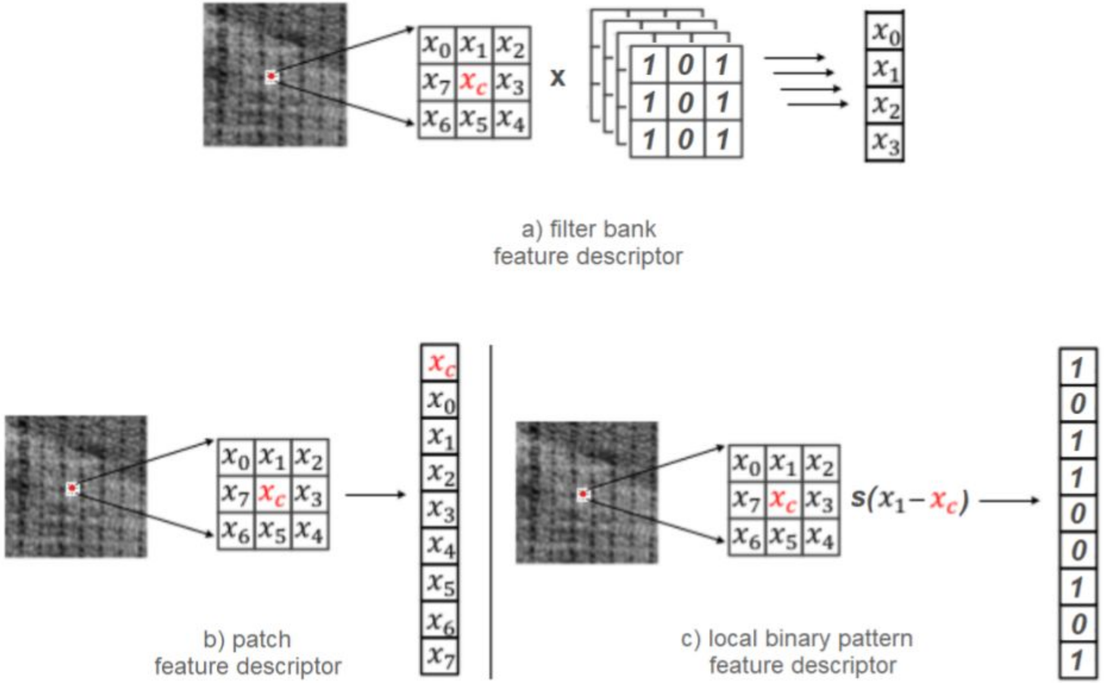
$$s(x) = \begin{cases} 1 & x \geq 0 \\ 0 & x < 0 \end{cases}$$

$$\mathrm{ELBP\_CI}_p(x_c) = s(x_c - \beta)$$

$$\mathrm{ELBP\_NI}_p(x_c) = \sum_{i=1}^{n^3} s(x_i - \beta_p)2^i$$

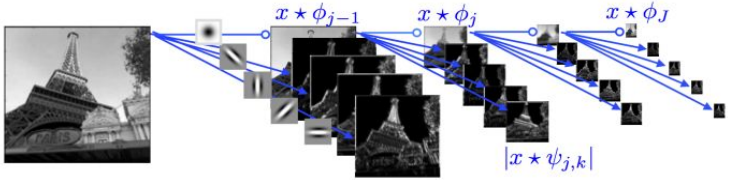
4. Methods: feature descriptors

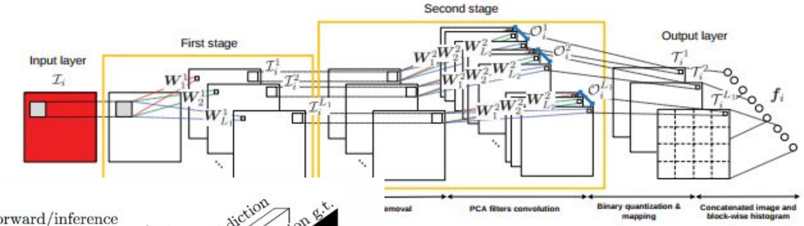
Shallow texture representations

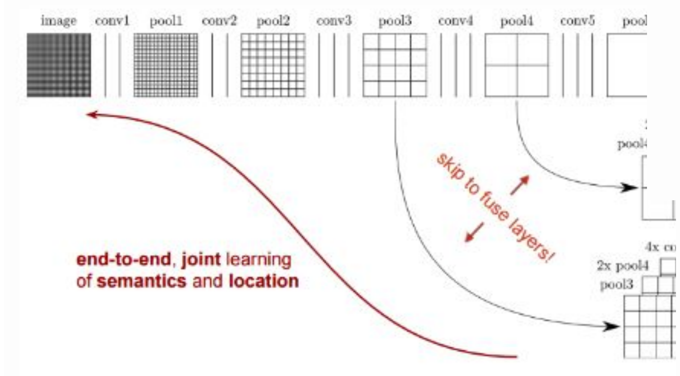


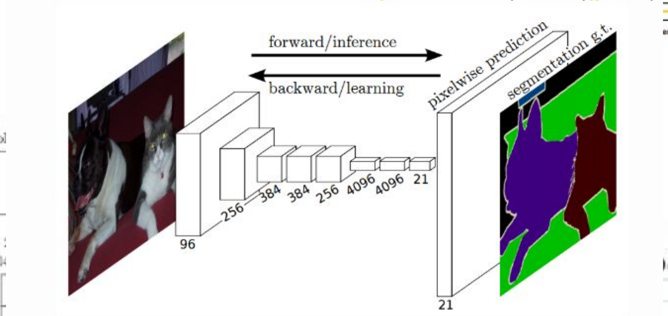
4. Methods
Deep texture representations

- allow for training from limited data
- capable of characterizing variation









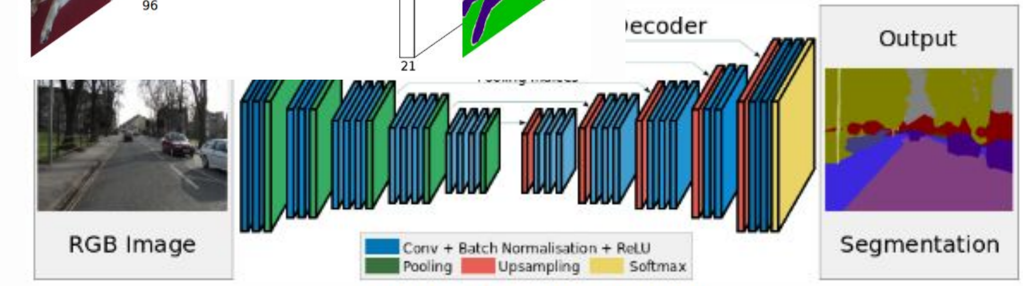


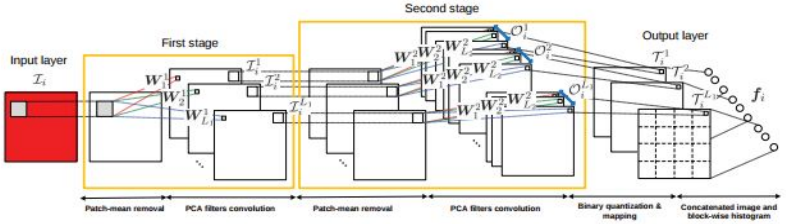
Figure : The SegNet Architecture

4. Methods
Deep texture representations

1. **transfer learning:** feature extractor
2. **hand-crafted nets:** random projections

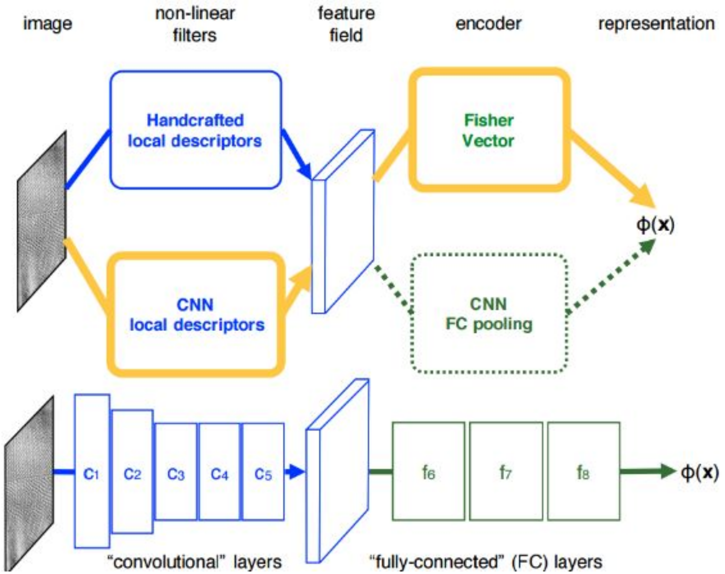
PCANet: A Simple Deep Learning Baseline for Image Classification?

Tsung-Han Chan, Kui Jia, Shenghua Gao, Jiwen Lu, Zinan Zeng, and Yi Ma



Deep Filter Banks for Texture Recognition and Segmentation

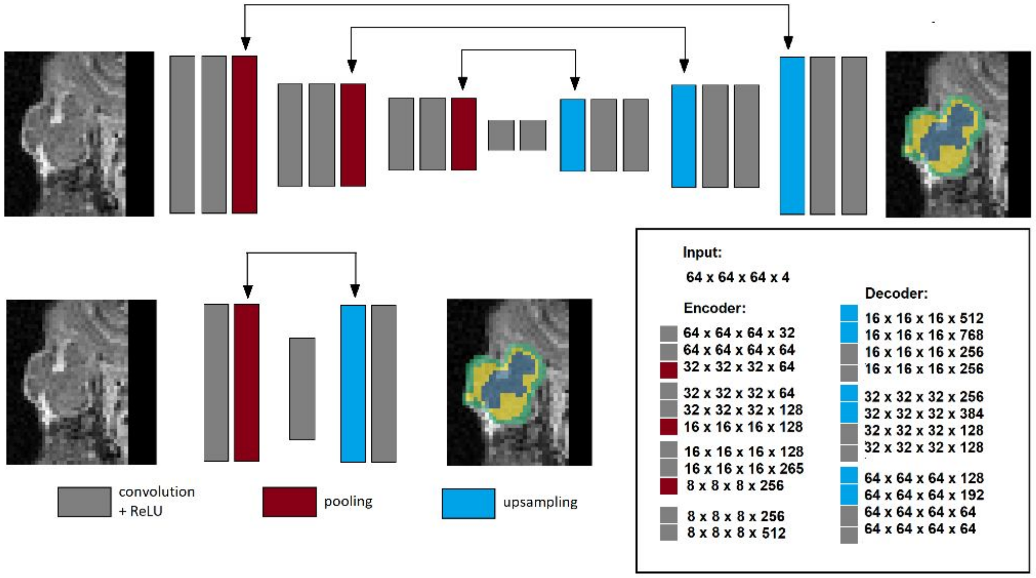
Mircea Cimpoi, University of Oxford
Subhransu Maji, University of Massachusetts, Amherst
Andrea Vedaldi, University of Oxford

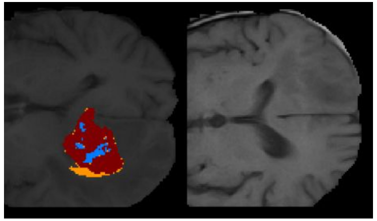


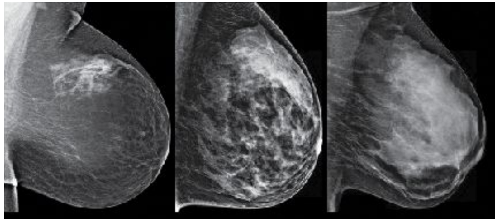
4. Methods
Deep texture representations

T-UNet

Rand-UNet

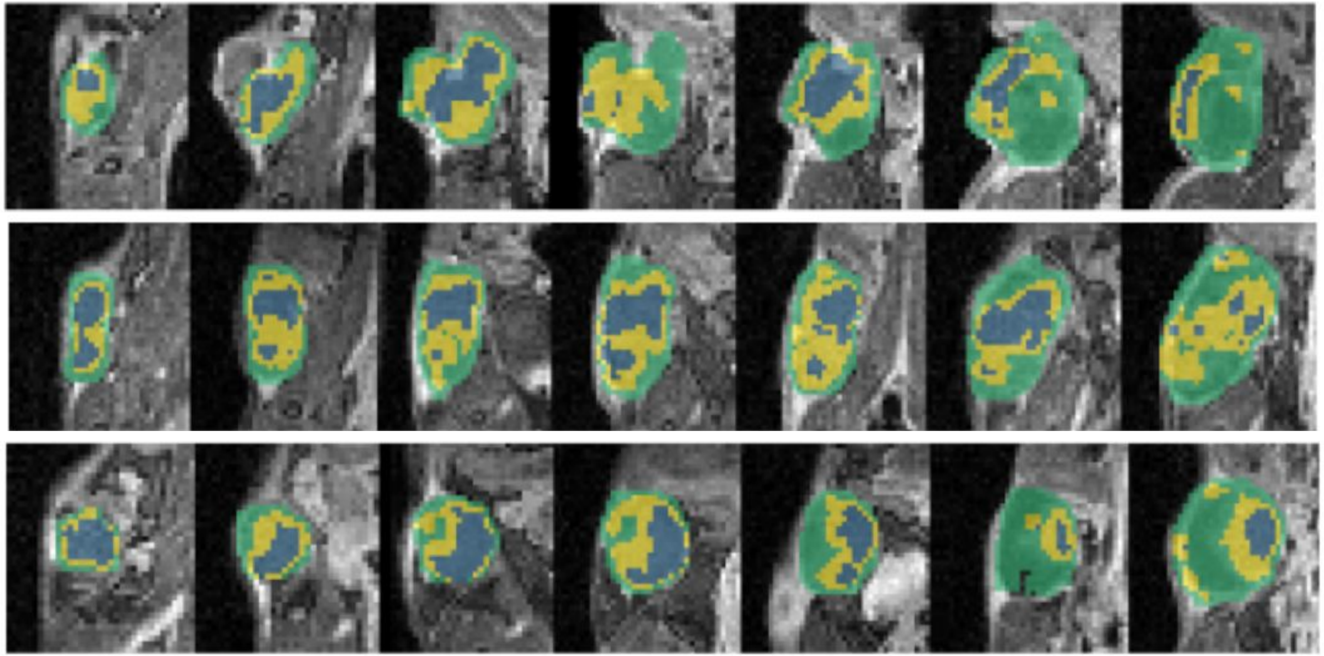


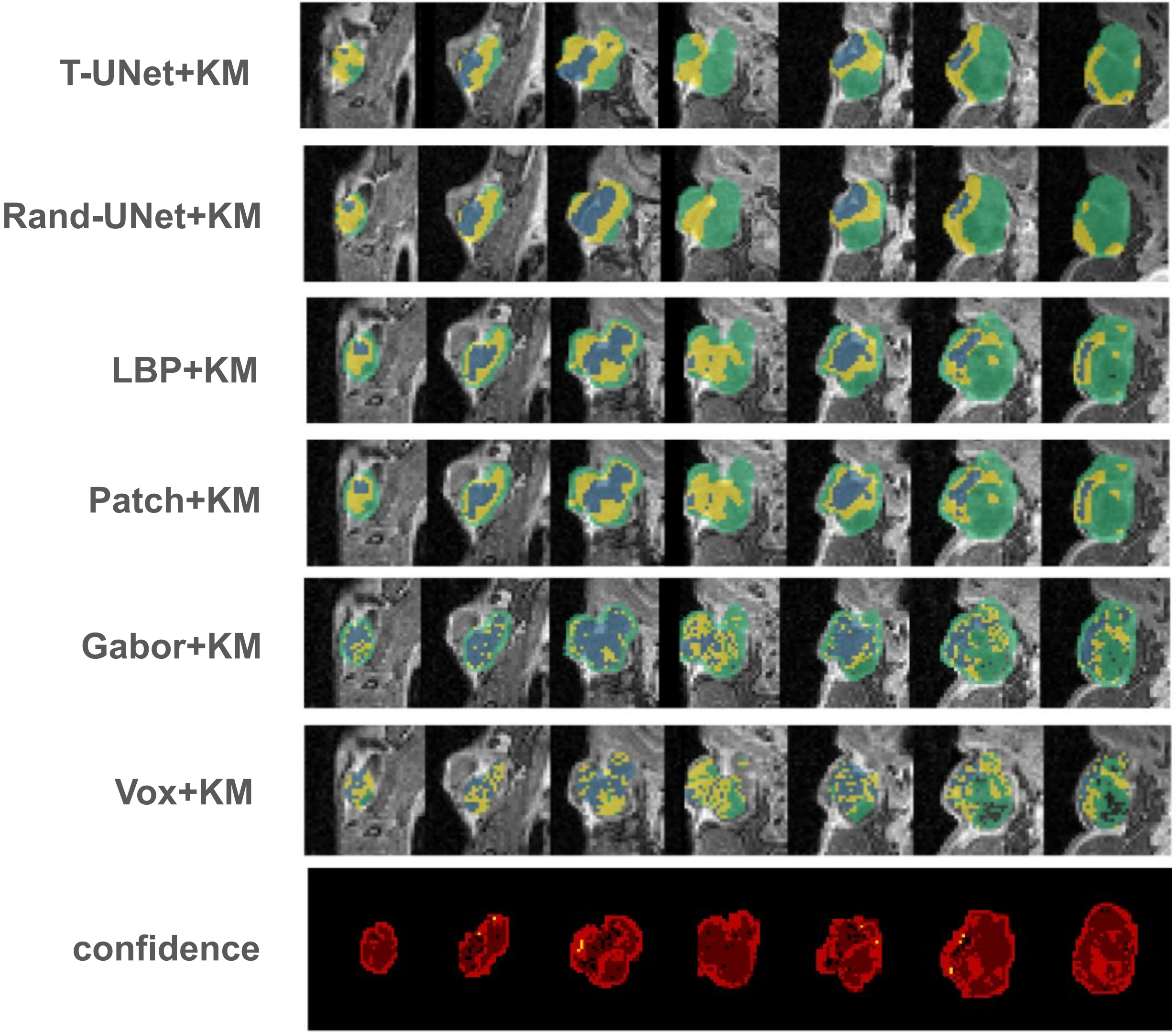




5. Results: segmentations

Pre-clinical: tumour progression




T-UNet+KM
Rand-UNet+KM
LBP+KM
Patch+KM
Gabor+KM
Vox+KM
confidence

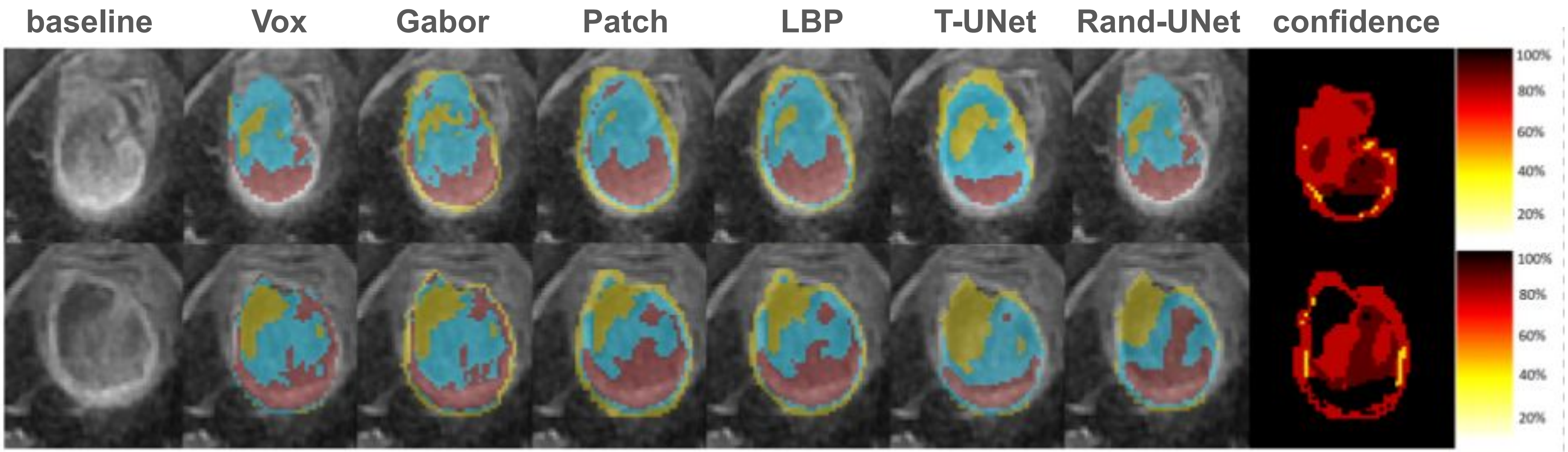
5. Results: classifications

Pre-clinical: tumour progression

	Vox	Filters	Patch	LBP	UNet	RandUNet
	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE	Acc. | DICE
KM	65% | 0.599	70% | 0.604	70% | 0.715	**75% | 0.723**	**80% | 0.825**	**75% | 0.729**
GMM	**82.5%** | 0.516	70% | 0.754	**70% | 0.958**	**70% | 0.963**	**77.5% | 0.783**	**75% | 0.715**

5. Results: segmentations

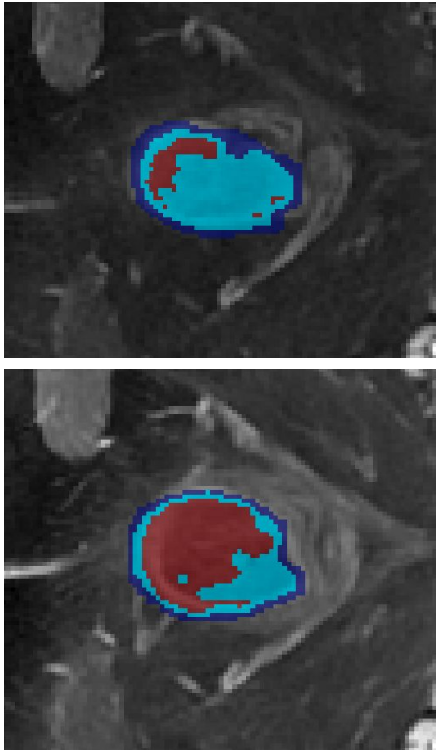
Clinical: therapy response

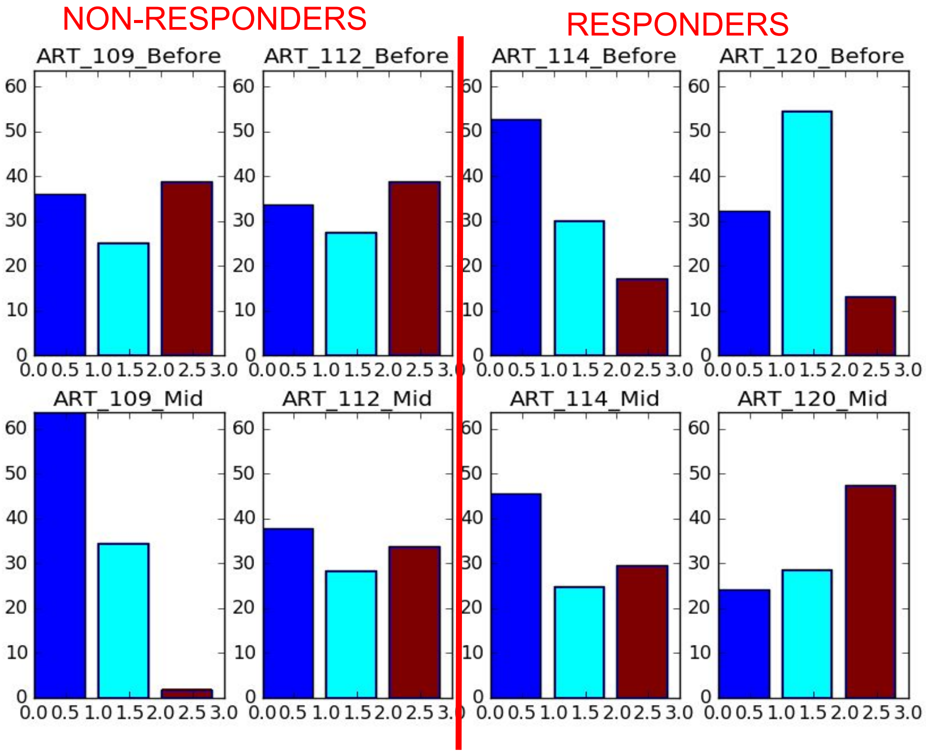


5. Results: classifications

Clinical: therapy response

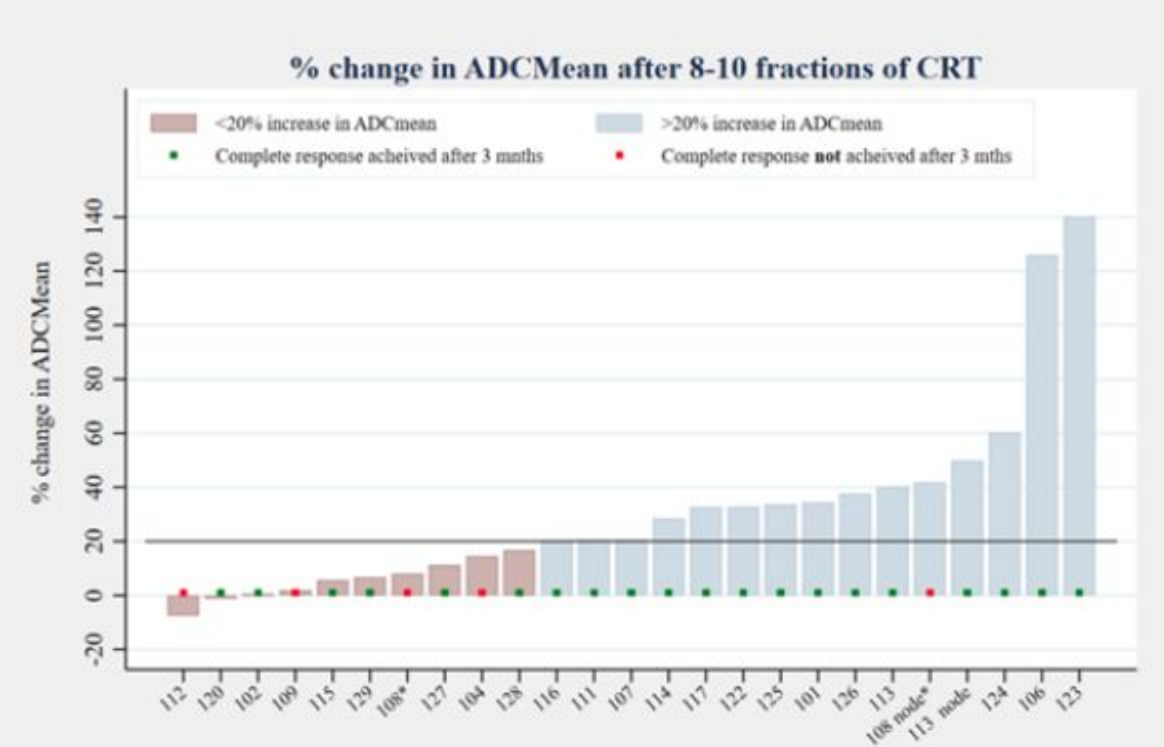
$$J\_SAD = \sum_{j=1}^{6} \sum_{i=0}^{k} abs(h_{j,1}(i) - h_{j,2}(i))$$





Part 1: Results

Question 2: Clinical application - therapy assessment

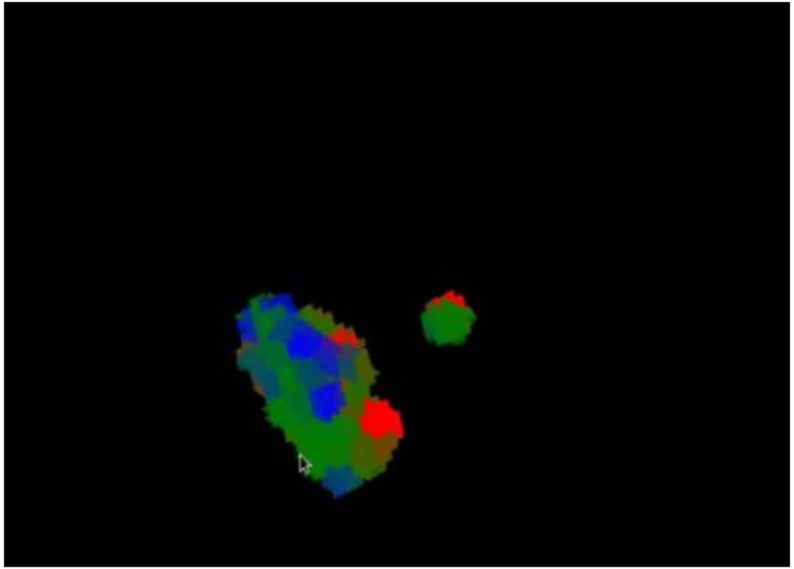


55

Quantifying Spatial Perfusion Heterogeneity in Tumours from DCE-MRI

Jola Mirecka
(jolanta.mirecka@eng.ox.ac.uk)

- ★ Collaborators: **Bartek Papiez, Benjamin Irving**
- ★ Pre-clinical collaborators: **Pavitra Kannan, Ana Gomes, Veerle Kesermans, Danny Allen, Paul Kinchesh, Sean Smart**
- ★ Clinical collaborators: **Ben George, Maria Hawkins**
- ★ Supervisors: **Mark Jenkinson, Julia Schnabel** and **Michael Chappell, Mike Brady** (advisory)



Questions?

CANCER RESEARCH UK
EPSRC

Cryo-EM?

- structure to function
- resolution revolution
- pharmaceutical implications

eBIC facilities

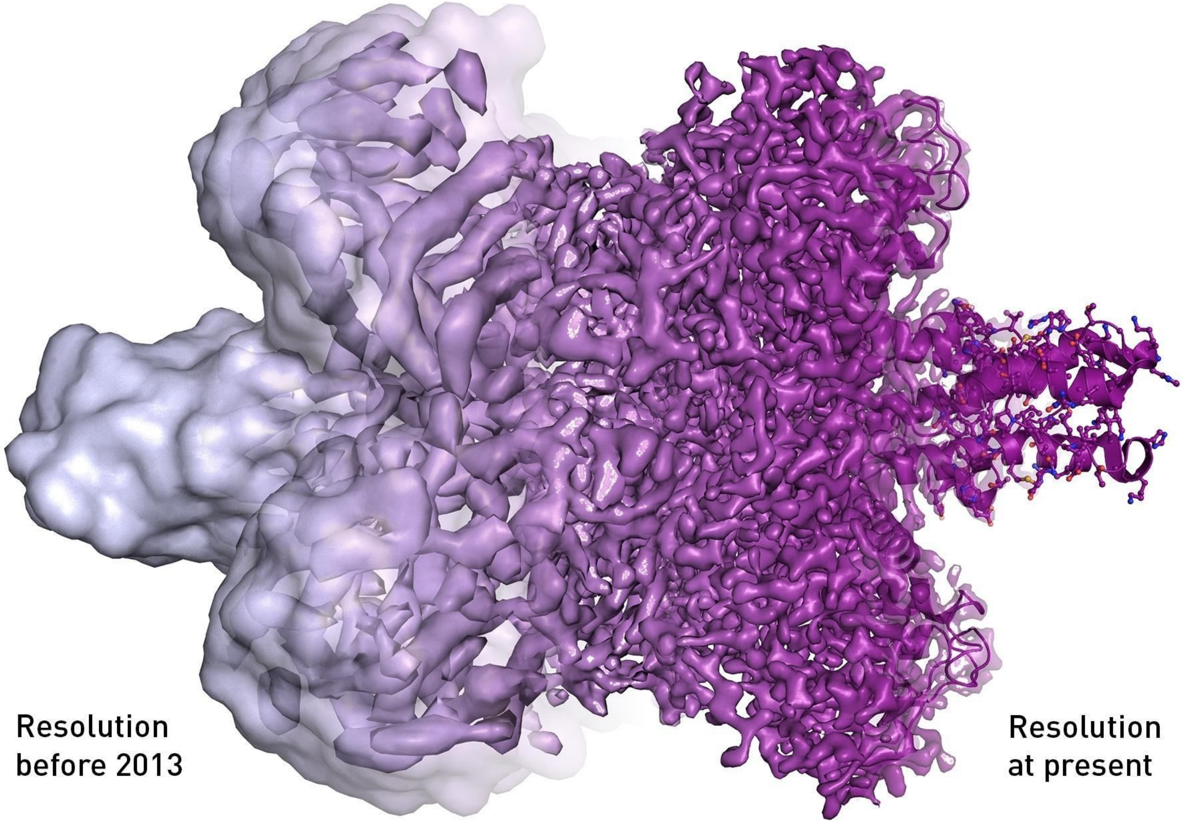
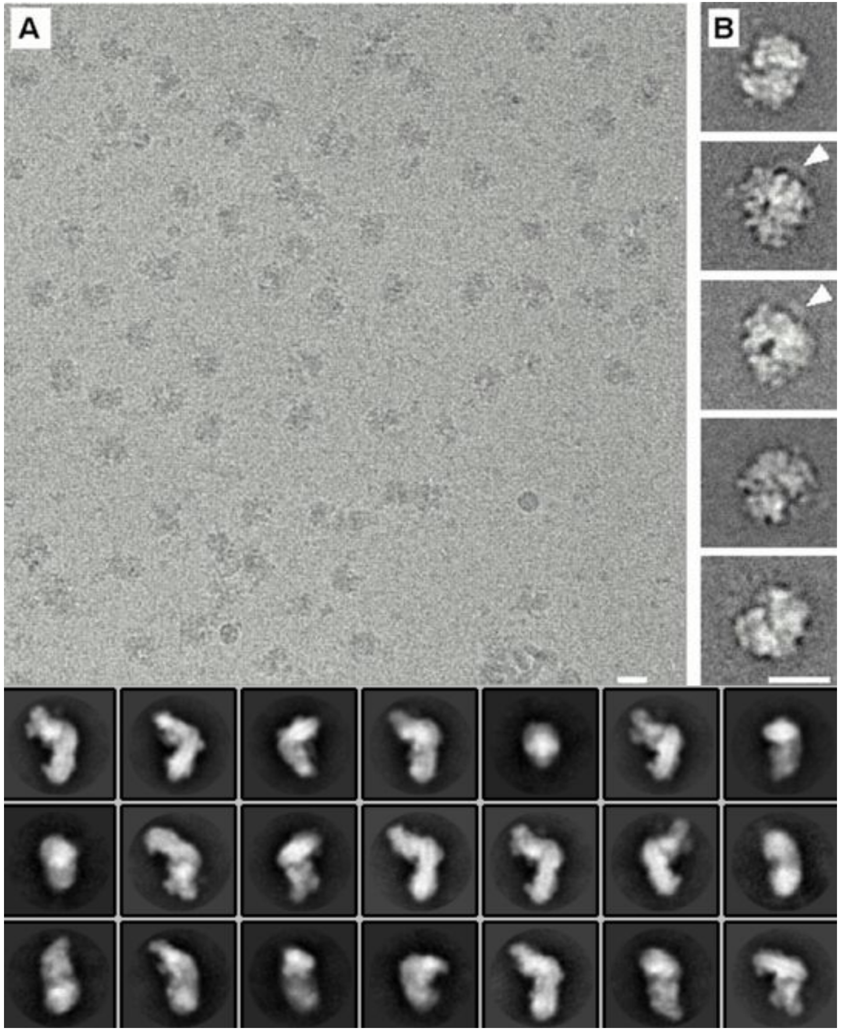


Illustration: ©Martin Högbom/The Royal Swedish Academy of Sciences

Cryo-EM?

Particle picking:

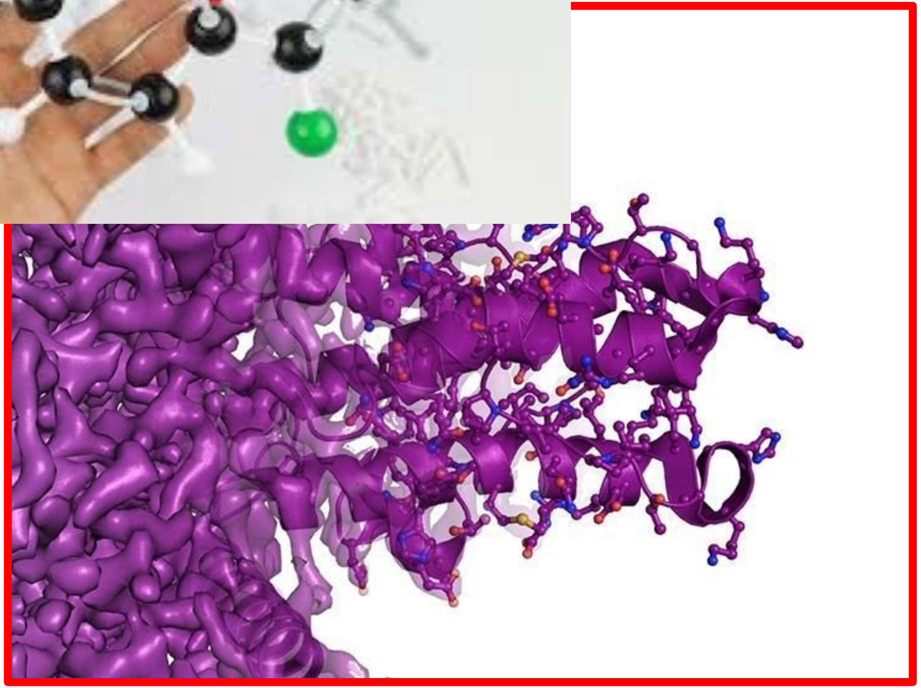
- noisy micrographs
- picking particles
- 2D classification



Cryo-EM?

Model building:

- density segmentation
- secondary structure
- side chains

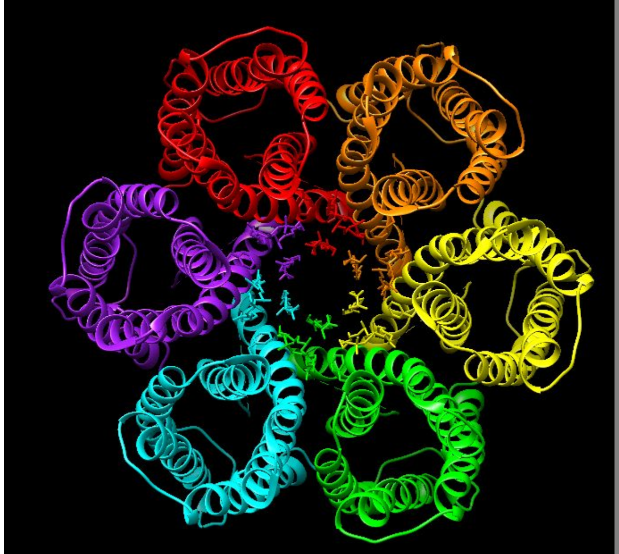


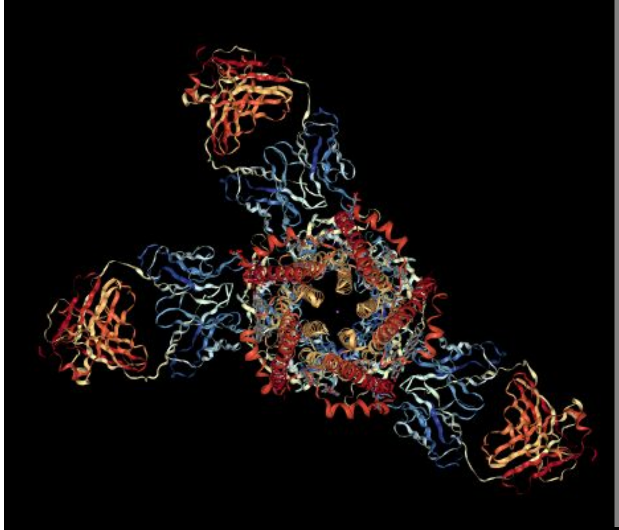
Cryo-EM?

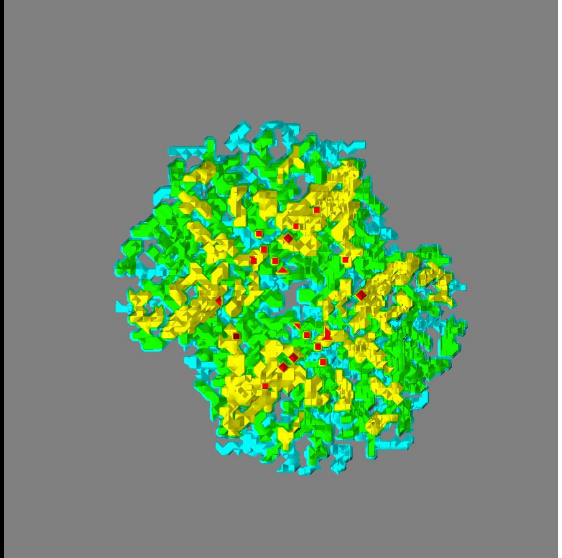
Model building:

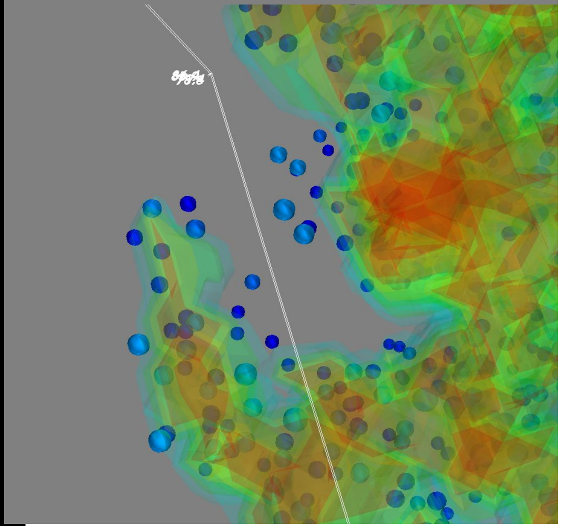
- density segmentation
- secondary structure
- side chains

Ribosome: 100 000 atoms





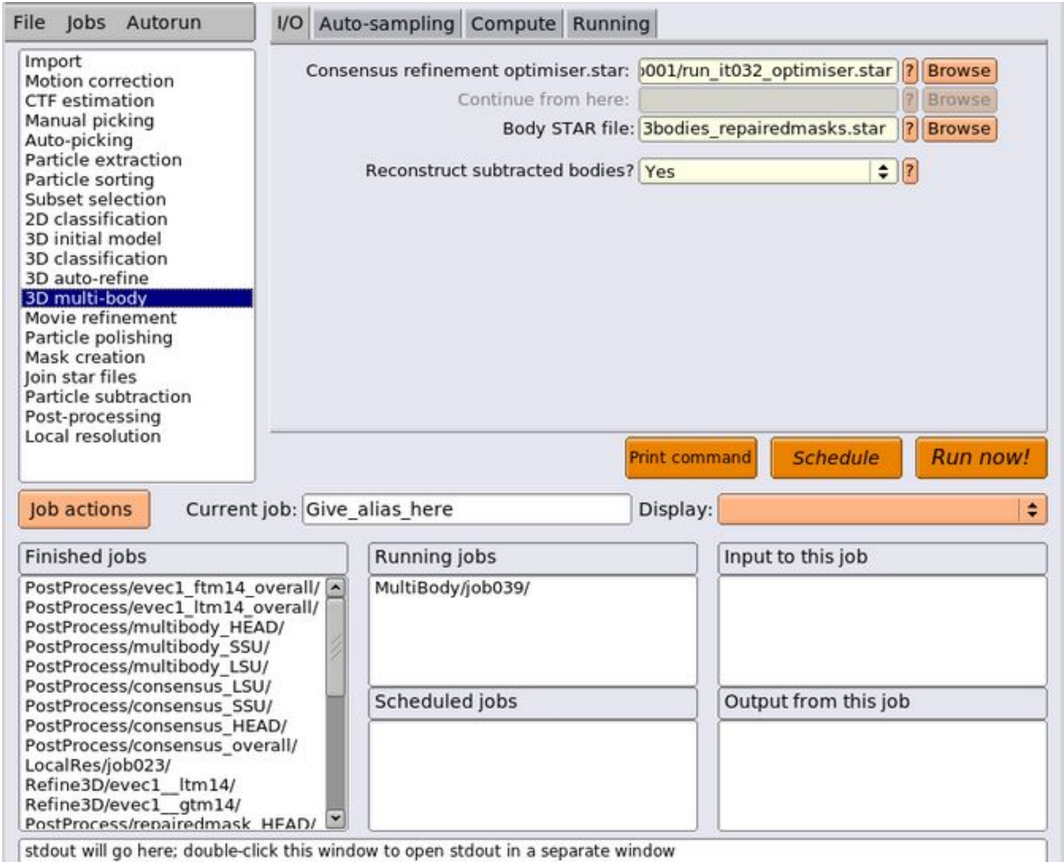




Cryo-EM?

Pipeline automation:

- automatic parameter selection
- data model



Questions?

CCP-EM:
Tom Burnley
Colin Palmer
Agnel Joseph
Martyn Winn

SciML:
Tony Hey
Jeyan Thiyagalingam