



Tumor regions and contrast-to-noise

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Radiography and image quality

Towards clinical application of renal dynamic contrast-enhanced MRI

Optimization of technical performance and evaluation of clinical feasibility

Eli Eikefjord



Dissertation for the degree of philosophiae doctor (PhD)
at the University of Bergen

2016

Dissertation date: 13.12.2016

A widely accepted definition of a **biomarker** is:

"a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes or a response to a therapeutic intervention"(4, p.13).

By combining the two concepts of quantitative MRI and biomarkers, a **quantitative imaging biomarker (QIB)** can be defined as "*an objectively measured characteristics derived from an *in vivo* image as an indicator of normal biological processes, pathogenic processes, or response to a therapeutic intervention*"(5, p. 814).

The development of QIBs must be based on the **understanding of the organ physiology** at the molecular level combined with the underlying **mechanisms of MRI signal generation and processing** into quantifiable values.

Sullivan et al*. (2015) emphasize the importance of establishing **technical performance** for a given biomarker prior to clinical validation studies in which **clinical performance** can be determined.

The **quality of an MR image** depends on the spatial resolution of the image and image contrast, the SNR, CNR, and the presence of artefacts.

When attempting to increase the imaging speed in [DCE]-MRI, it is important to retain acceptable image quality and **diagnostic capability**.

Radiography and image quality and metrology

"the scientific study of measurement"

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Recommended Terminology for Describing the Technical Performance of QIBs

Term	Definition
QIB	A characteristic derived from one or more in vivo images and objectively measured according to a ratio or interval scale as an indicator of normal biological processes, pathogenic processes, or response to a therapeutic intervention.
Measurand	The quantity intended to be measured (VIM clause 2.3).
Bias	An estimate of a systematic measurement error (VIM clause 2.18).
Linearity	The ability to provide measured quantity values that are directly proportional to the value of the measurand in the experimental unit (ISO standard 18113).
Precision	The closeness of agreement between measured quantity values obtained by means of replicate measurements of the same or similar experimental units with specified conditions (VIM clause 2.15). Repeatability and reproducibility are types of precision.
Reference value	A value, generally accepted as having a suitably small measurement uncertainty, to be used as a basis for comparison with values of quantities of the same kind (eg, the mean of a large number of replicate measurements) by using a reference method (VIM clause 5.18).
Repeatability	The measurement precision with conditions that remain unchanged between replicate measurements (repeatability conditions) (VIM clause 2.20).
Repeatability conditions	The set of conditions that includes the same measurement procedure, same operators, same measuring system, same operating conditions, same physical location, and replicate measurements of the same or similar experimental units over a short period of time.
Reproducibility	The measurement precision with conditions that vary between replicate measurements (reproducibility conditions) (VIM clause 2.25).
Reproducibility conditions	The set of conditions that includes (a) different locations, operators, and measuring systems and (b) replicate measurements of the same or similar objects.
Truth or true value	In metrology, truth is the real or actual value of a quantity associated with some object. Because each physical measurement has some uncertainty in terms of whether it agrees with the real quantity value, the true value cannot be known with certainty.

Note.—ISO = International Organization for Standardization, VIM = International Vocabulary of Metrology.

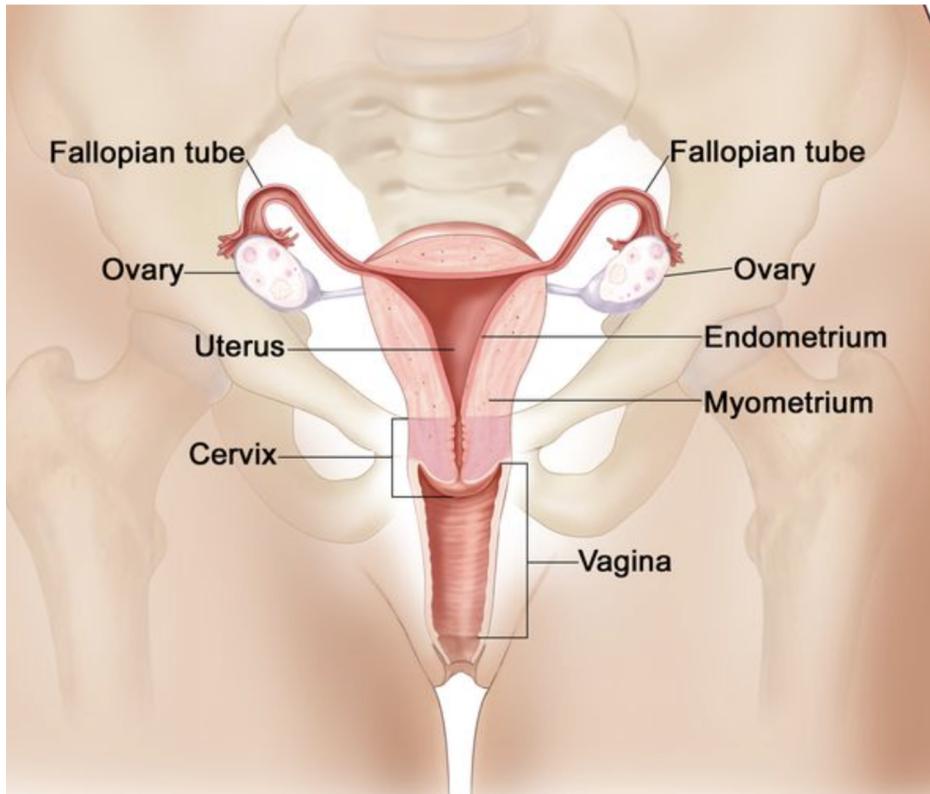
Context & aims:

- Local assessment of segmentation uncertainty (confidence)
- Assessment of inter-observer variability
- MR sequence-specific performance / detection ability
- Stochastic optimization with energy terms expressing:
 - (i) 1D signal intensity gradient strength
 - (ii) Shape smoothness
- Radiomics / texture-to-noise (TNR)

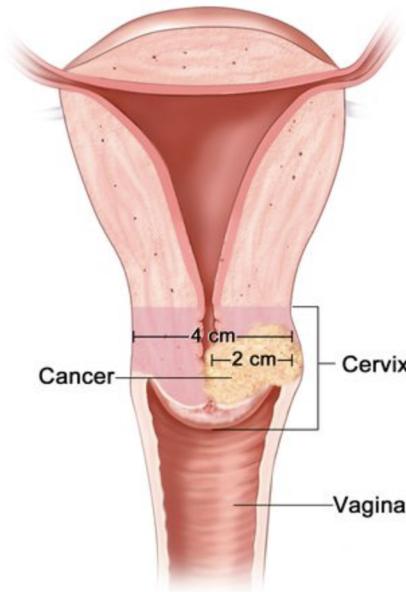


Cervical cancer

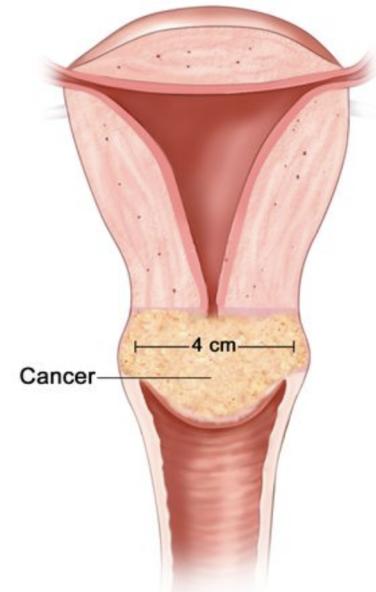
Cervical cancer

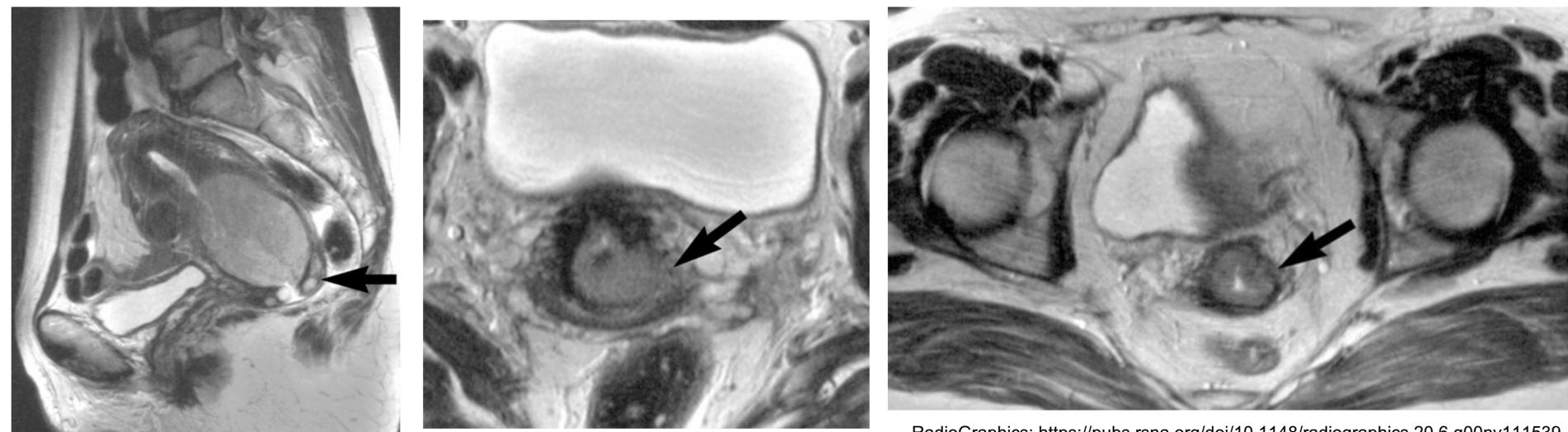


Stage IB2 Cervical Cancer

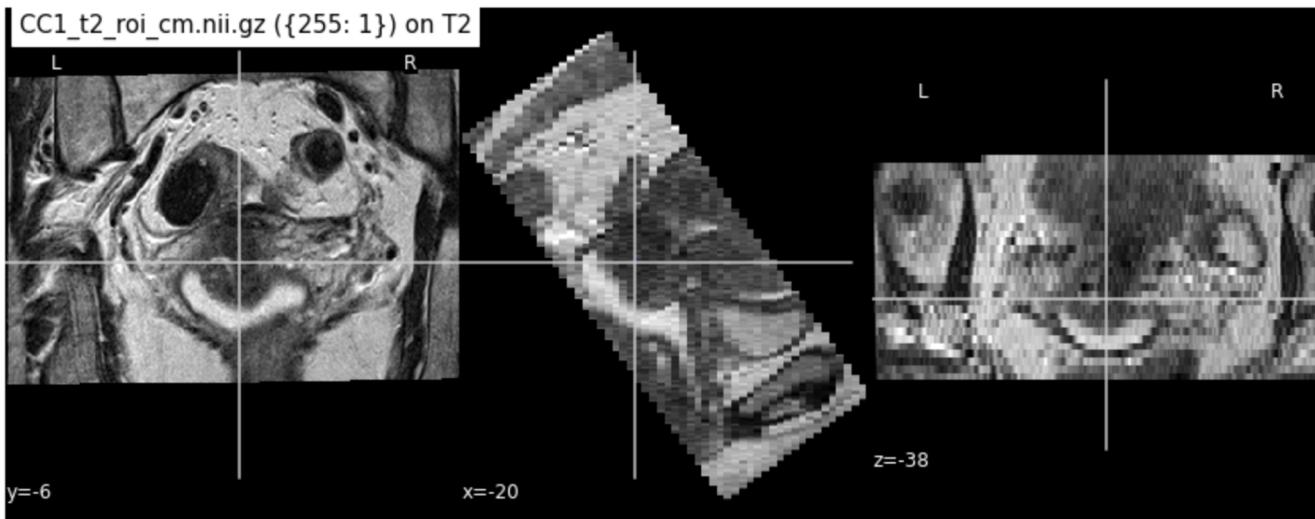


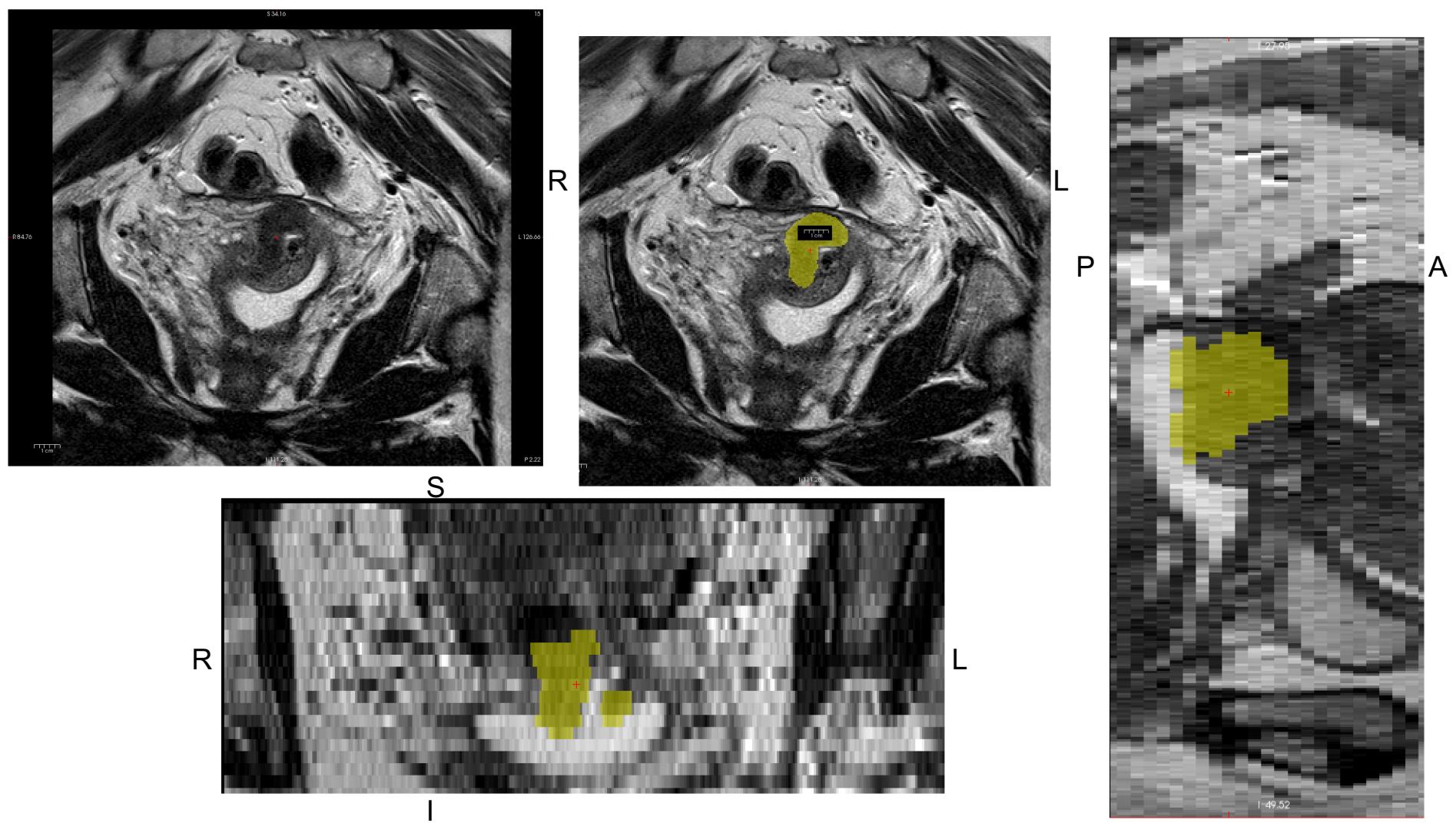
Stage IB3 Cervical Cancer

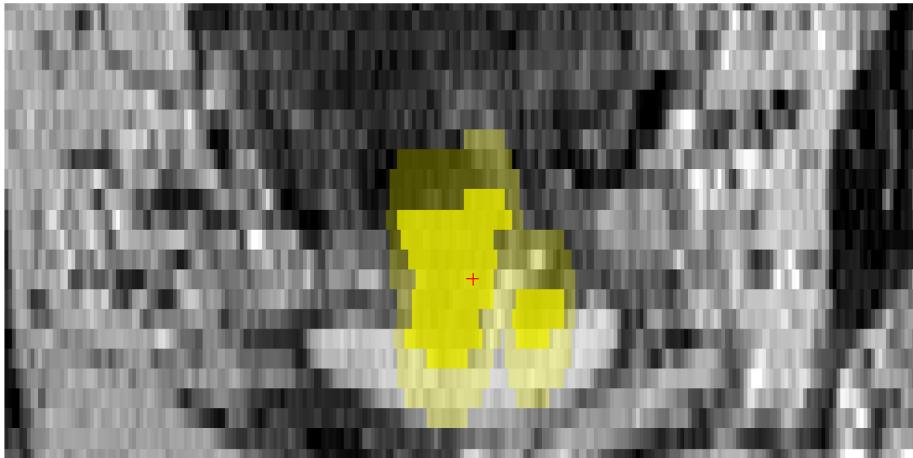
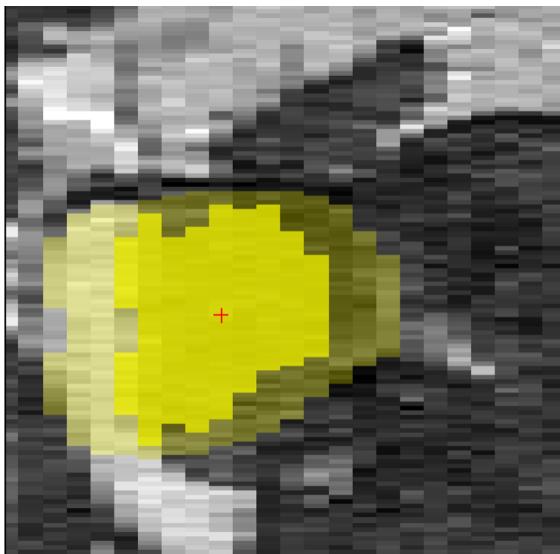
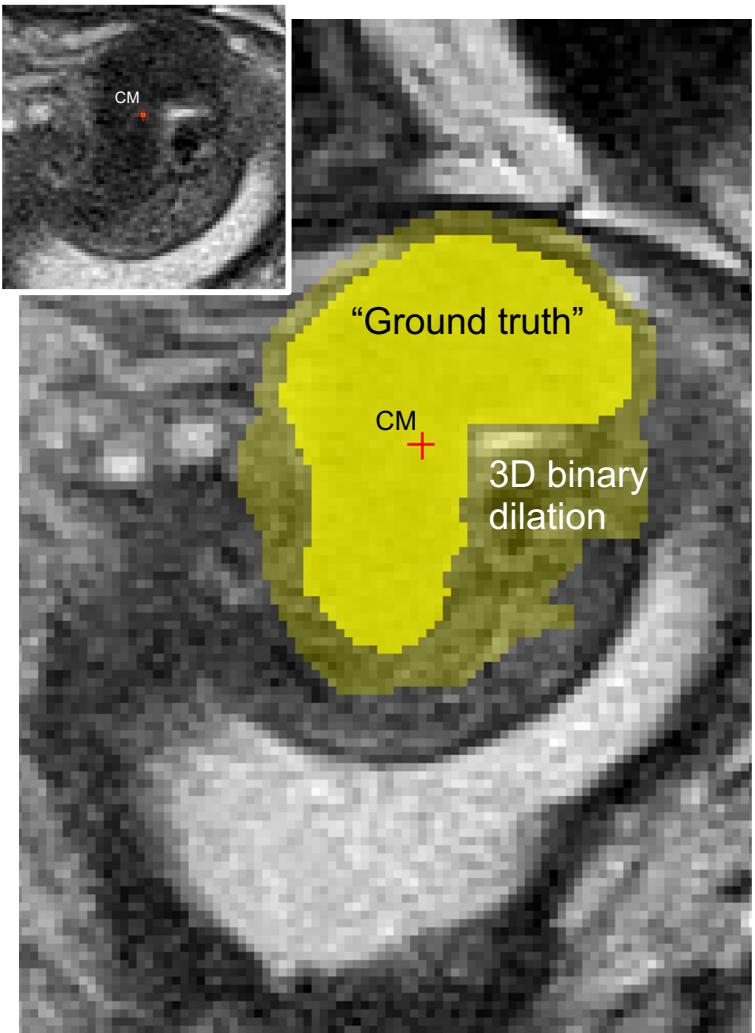




RadioGraphics: <https://pubs.rsna.org/doi/10.1148/radiographics.20.6.g00nv111539>







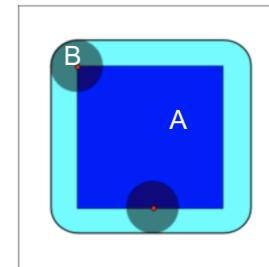
Signal intensity in
tumor region and
surrounding tissue
(how to define?)

3D morphological dilation of ROI

The dilation of A by B is defined by

$$A \oplus B = \bigcup_{b \in B} A_b,$$

where A_b is the translation of A by b .



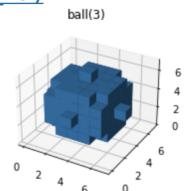
The dilation of a dark-blue square (A) by a disk (B), resulting in the light-blue square with rounded corners.

If B has a center on the origin, then the dilation of A by B can be understood as the locus of the points covered by B when the center of B moves inside A .

- Wikipedia Dilation_(morphology) - [https://en.m.wikipedia.org/wiki/Dilation_\(morphology\)](https://en.m.wikipedia.org/wiki/Dilation_(morphology))
- Introduction to three-dimensional image processing - https://scikit-image.org skimage-tutorials/lectures/three_dimensional_image_processing.html
- scipy.ndimage.morphology.binary_dilation - https://docs.scipy.org/doc/scipy-0.14.0/reference/generated/scipy.ndimage.morphology.binary_dilation.html
- Morphological Transformations (OpenCV) - https://opencv24-python-tutorials.readthedocs.io/en/latest/py_tutorials/py_imgproc/py_morphological_ops/py_morphological_ops.html
- Dilating a 3D region in MRI - <https://stackoverflow.com/questions/62412913/how-to-speed-up-dilating-a-3d-region-in-a-boolean-numpy-array>
- Julia Morphological operations - https://juliaimages.org/dev/examples/image_morphology/image_morphology
- Scikit-Image morphology - <https://scikit-image.org/docs/dev/api/skimage.morphology.html>

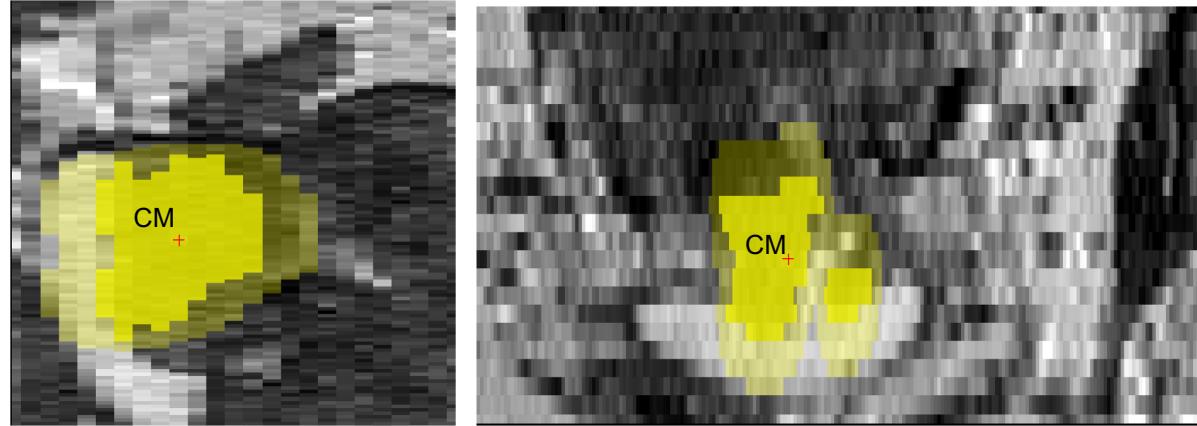
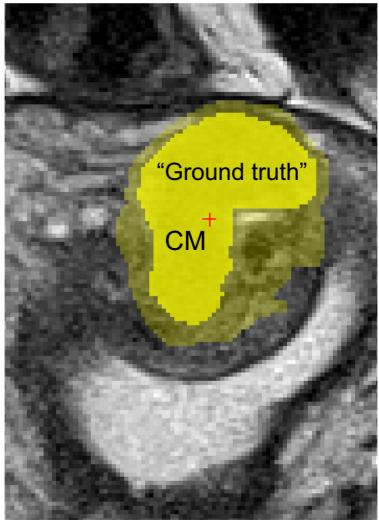
```
subj = 'CC1'  
file_ROI = f'{res_dir}/{subj}_t2_roi.nii.gz'  
roi = nib.load(file_ROI)  
mask3d = roi.get_fdata()  
roi_header = roi.header  
roi_affine = roi.affine
```

```
from scipy import ndimage as ndi  
nr = 3  
dilated = ndi.binary_dilation(mask3d, structure = ball(radius=nr))  
  
roi_dilated = nib.nifti1.Nifti1Image(dilated.astype(np.bool_),  
                                      affine=roi_affine,  
                                      header=roi_header)  
file_ROI_dilated = f'{res_dir}/{subj}_t2_roi_dilated_ball{nr}.nii.gz'  
nib.save(roi_dilated, file_ROI_dilated)
```



Structuring element:

ROI center of mass (CM)



```
subj = 'CC1'  
file_ROI = f'{res_dir}/{subj}_t2_roi.nii.gz'  
roi = nib.load(file_ROI)  
mask3d = roi.get_fdata()  
roi_header = roi.header  
roi_affine = roi.affine
```

```
non0 = np.argwhere(mask3d > 0)      # Find all non-zero voxels in 3D ROI  
# Get the mean (i,j,k) coordinate location of these non0 voxels  
CM_bin = list(np.average(non0[:, :], axis=0).round(0).astype(np.uint8))  
print(f'CM_bin: {CM_bin}')  
CM_bin: [156, 174, 15]
```

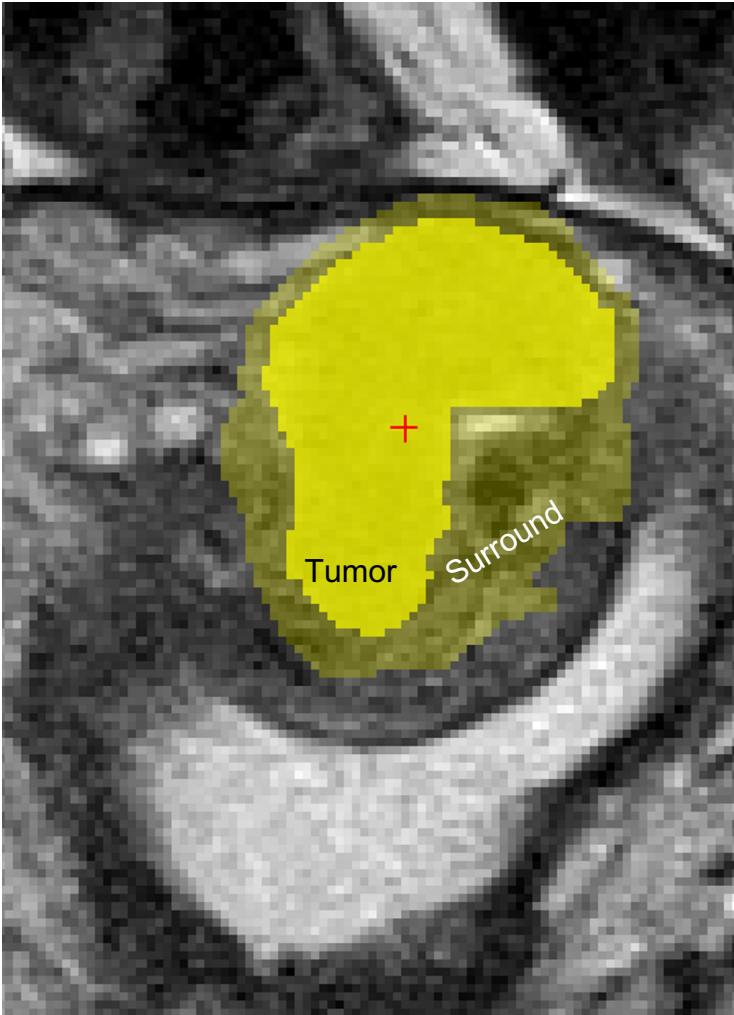
Scanner (x,y,z) vs. Image (i,j,k) and homogeneous coordinates

RAS = Right-Anterior-Superior

vox2ras(roi, CM_bin)

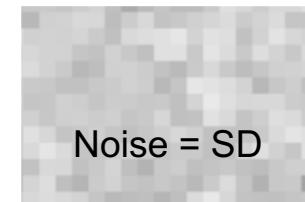
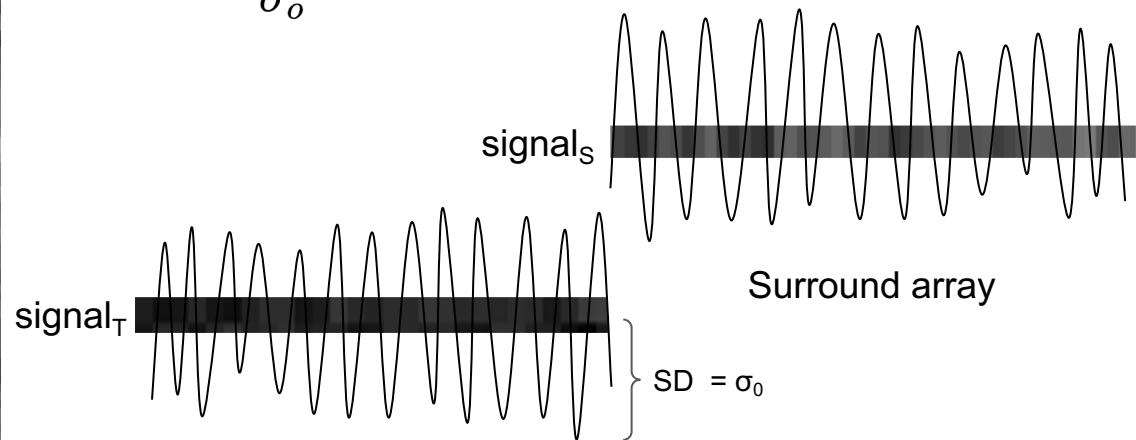
→ [-20.95, -6.84, -38.56]

```
def vox2ras(nifti, ijk):  
    ...  
    Applying the affine (https://nipy.org/nibabel/coordinate\_systems.html)  
    To make the affine simpler to apply, we split it into M and (a,b,c)  
    Return X, Y, Z coordinates for voxel location ijk with coordinates [i, j, k]  
    ...  
    M = nifti.affine[:3, :3]  
    abc = nifti.affine[:3, 3]  
  
    return list(M.dot([ijk[0], ijk[1], ijk[2]]) + abc)
```

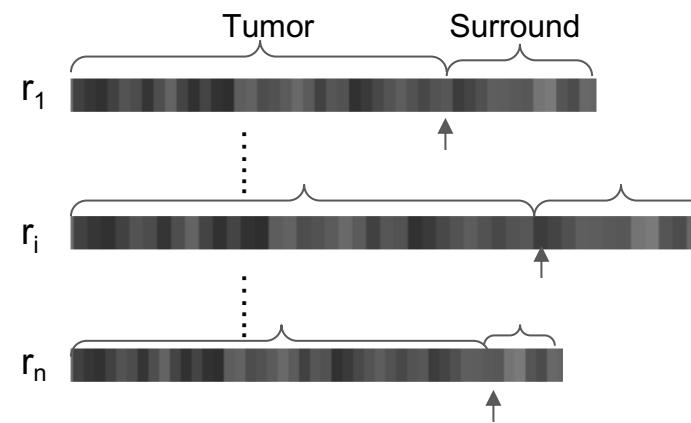
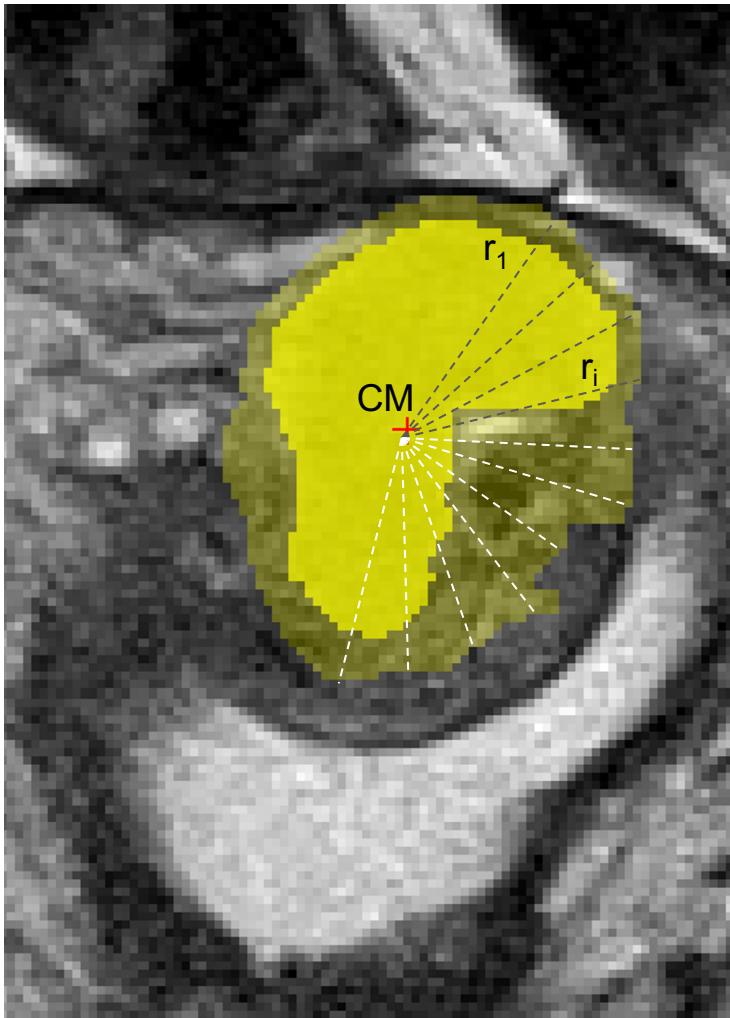


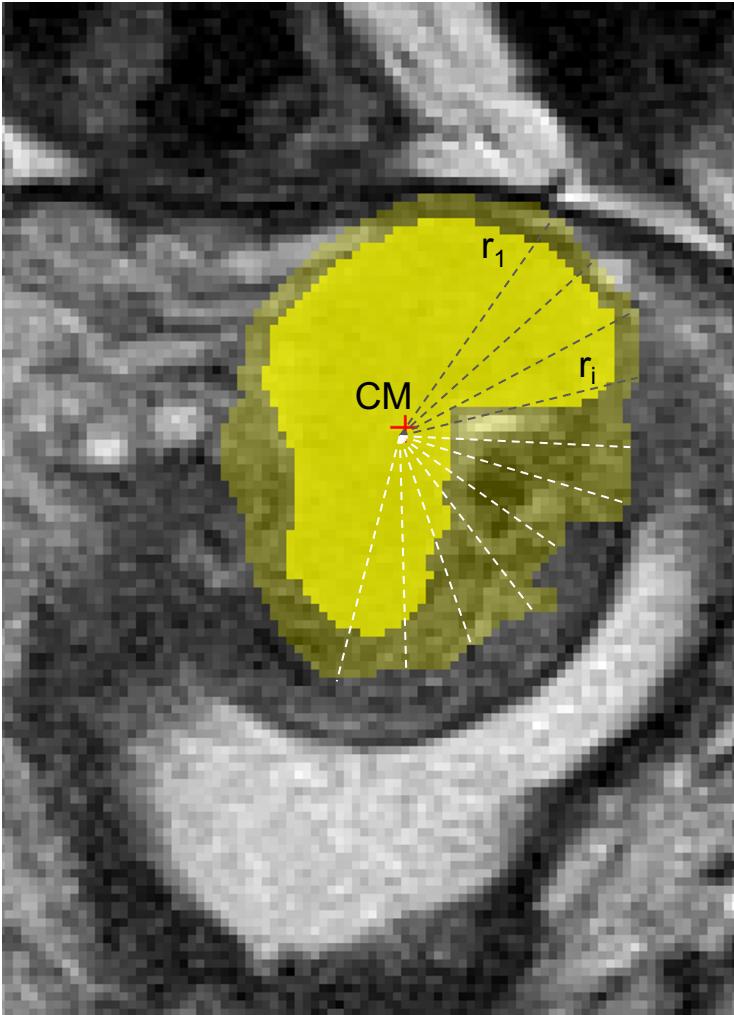
Contrast-to-noise (tumor / surround)

$$C = \frac{|S_A - S_B|}{\sigma_o}$$



Radial CNR





Radial CNR cont.



Geir Storvik

Professor in Statistics, University of Oslo

Verifieret e-postadresse på math.uio.no

Statistical computing spatio-temporal processes statistical ecology

A Bayesian approach to dynamic contours through stochastic sampling and simulated annealing.
IEEE-PAMI 1994;16(10):976-986 [[link](#)] [[pdf](#)]

A. Lundervold and T. Taxt. Automatic detection of left ventricular cardiac boundary.
In NOBIM Conference, Tromsø, May 1990. (implementing Friedman & Adam, 1989)

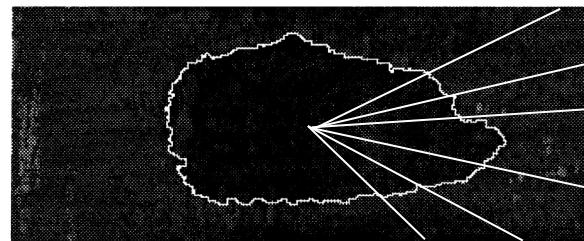
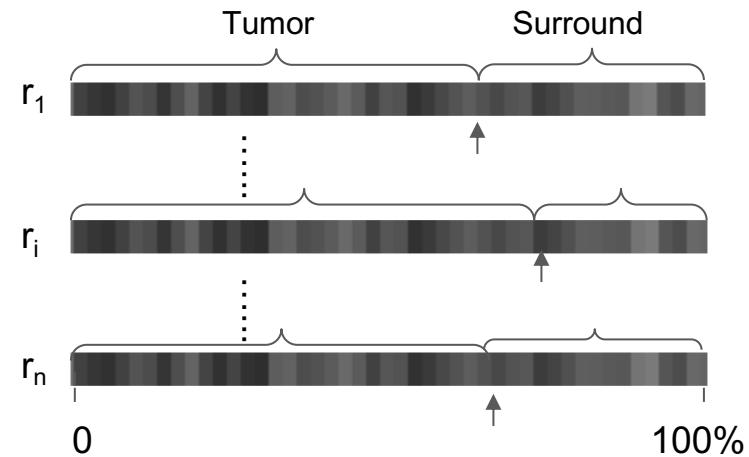
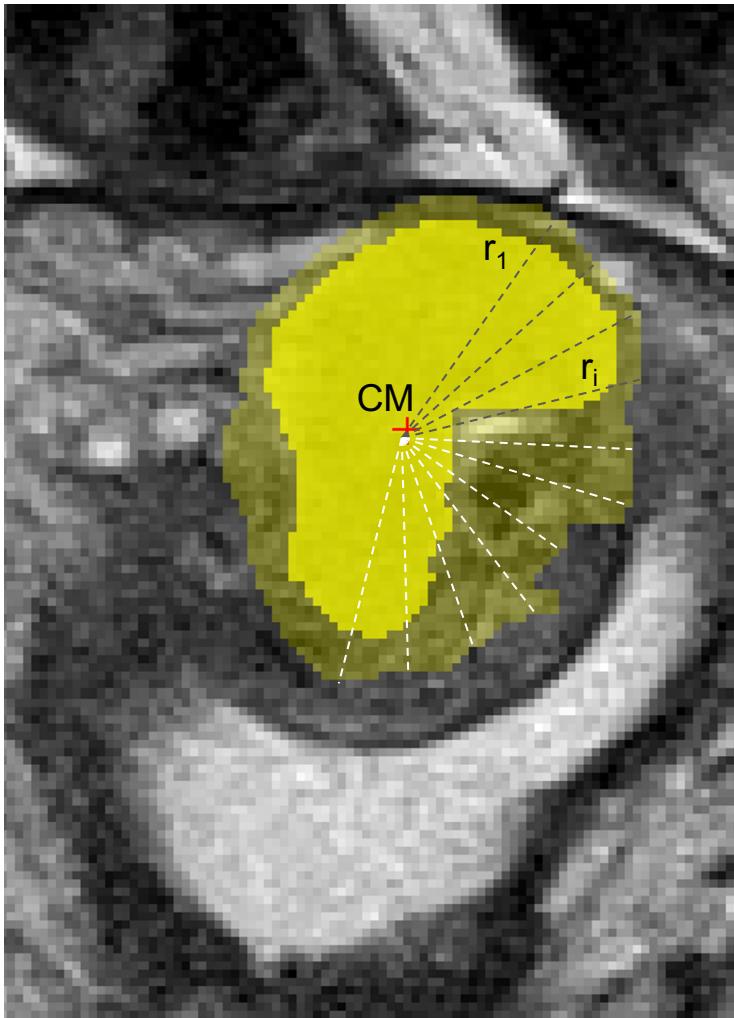
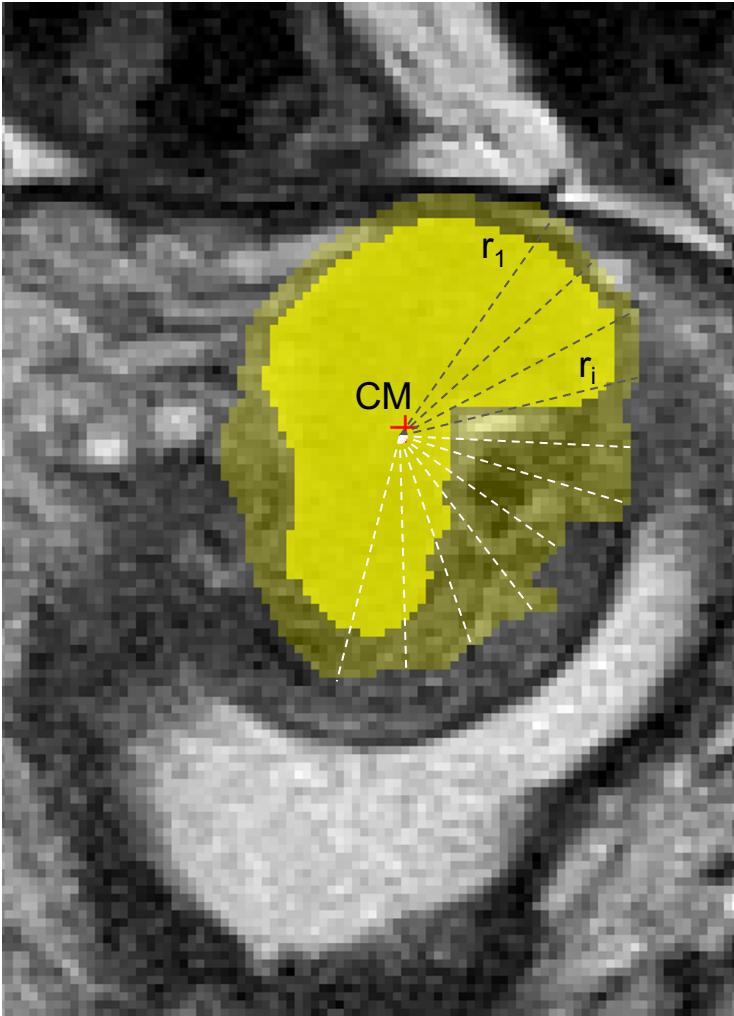


Figure 6: Restoration of the ultrasound image of left ventricular cavity.

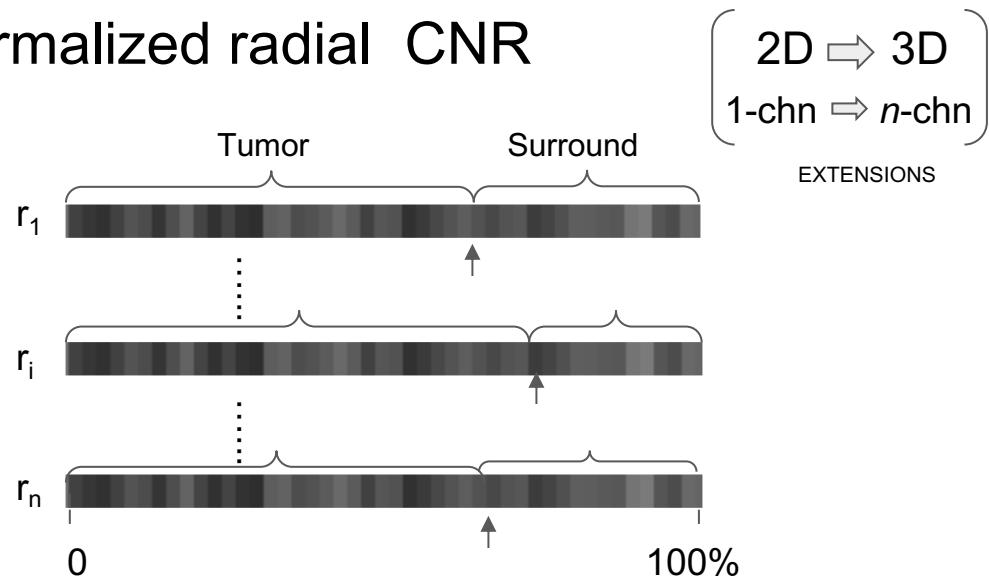
Friedman N & Adam D. Automatic ventricular cavity boundary detection from sequential ultrasound images using simulated annealing. IEEE-TMI 1989;8(4):344-353 <https://ieeexplore.ieee.org/document/41487>

Normalized radial CNR





Normalized radial CNR



Purpose / aims:

- Local assessment of segmentation uncertainty (confidence)
- Assessment of inter-observer variability
- MR sequence-specific performance / detection ability
- Stochastic optimization with energy terms expressing:
 - (i) 1D signal intensity gradient strength (where to set the ↑)
 - (ii) Shape smoothness - length differences between neighbouring radii
- Radiomics / texture-to-noise (TNR)

THANKS !