



# Artificial intelligence in MR image analysis

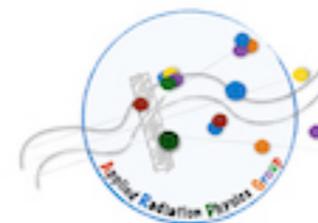
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Artificial Intelligence in Medicine  
Sapienza Università di Roma Dip. Di Fisica  
Aula Conversi 3 dicembre 2018



SAPIENZA  
UNIVERSITÀ DI ROMA



INFN

# Outline

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- Brief introduction
- Description of the software tool we developed
- An introduction to Deep Learning applied to this problem

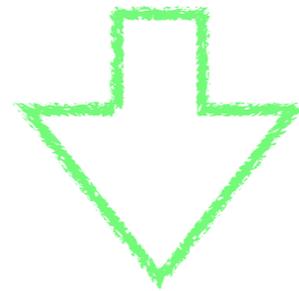


# Brief introduction

# Introduction

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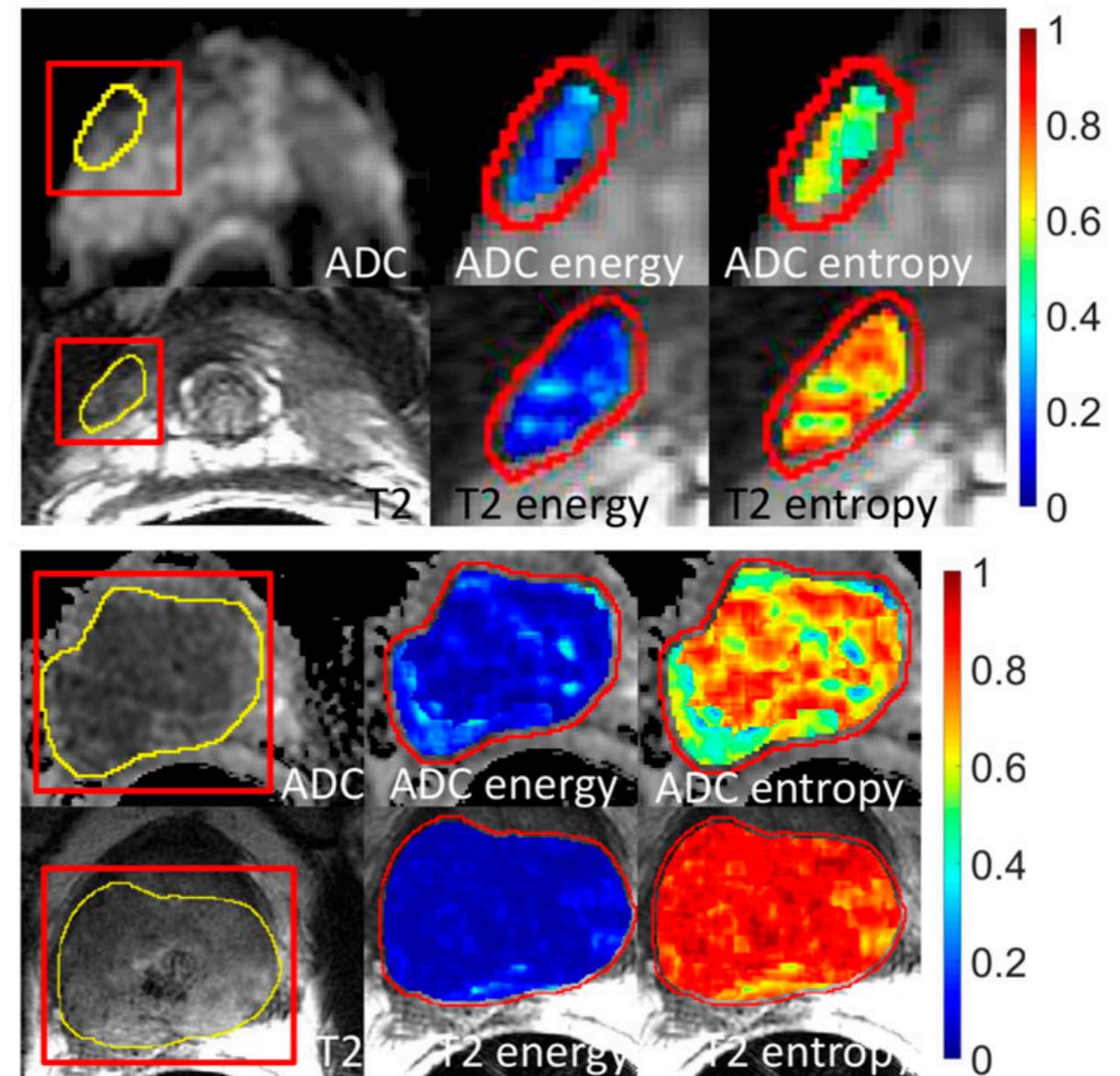
- The therapy for locally advanced rectal cancers is:
  - neoadjuvant chemo-radiotherapy (CRT)
  - followed by radical surgery



- local pelvic recurrence to rate lower than 10%

# Application on prostate cancer

- machine learning-based automatic classification of prostate cancer aggressiveness
- combining apparent diffusion coefficient (ADC) and T2- weighted (T2-w) MRI-based texture features
- achieved an accuracy greater than 90%



D. Fehr et al. "Automatic classification of prostate cancer Gleason scores from multiparametric magnetic resonance images," Proc Natl Acad Sci USA, vol. 112, no. 46, pp. E6265–E6273, Nov. 2015.

# However...

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- This therapeutic approach is an **over-treatment** of many patients:
- those who do not respond to the treatment (non-responders)
  - whose early identification (2–3 weeks after the start of neoadjuvant CRT) might help clinicians in referring them to alternative treatments;
- patients with pathological complete response
  - who could benefit from either less invasive surgery (ie, transanal endoscopic microsurgery) or “wait-and-watch” strategy

# The purpose

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- Recognise non-responders and complete responder patients during the CRT (before surgery)

# MaRIANNe

## MAgnetic Resonance Image Analysis with Neural NEtworks

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- Project proposed to Lazio Region funding scheme  
“Progetti Gruppi di Ricerca, Conoscenza e cooperazione per un nuovo modello di sviluppo (L.R. 13/2008 - art. 4)” del Programma Strategico regionale per la ricerca, l’innovazione ed il trasferimento tecnologico della Regione Lazio”
- Leded by ISS, PI: Paolo Del Giudice
- Collaboration with:
  - INFN-Roma1 and Roma3
  - CNR-ISC
  - Umberto I San Camillo-Forlanini and Sant’Andrea
- With the endorsement of 4 private companies (one of them is IBM)
- Positively assessed but not granted

The software tool we developed

# Software tool

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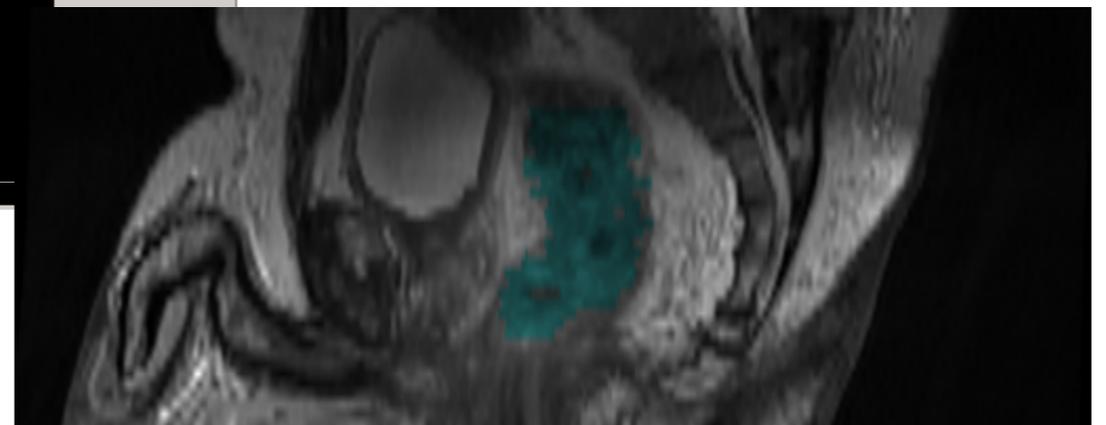
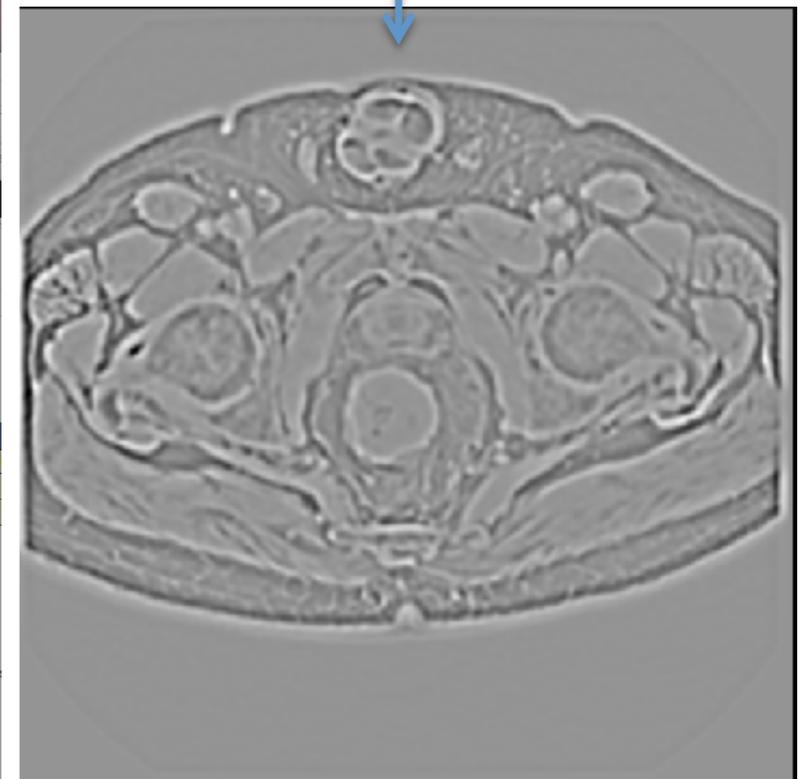
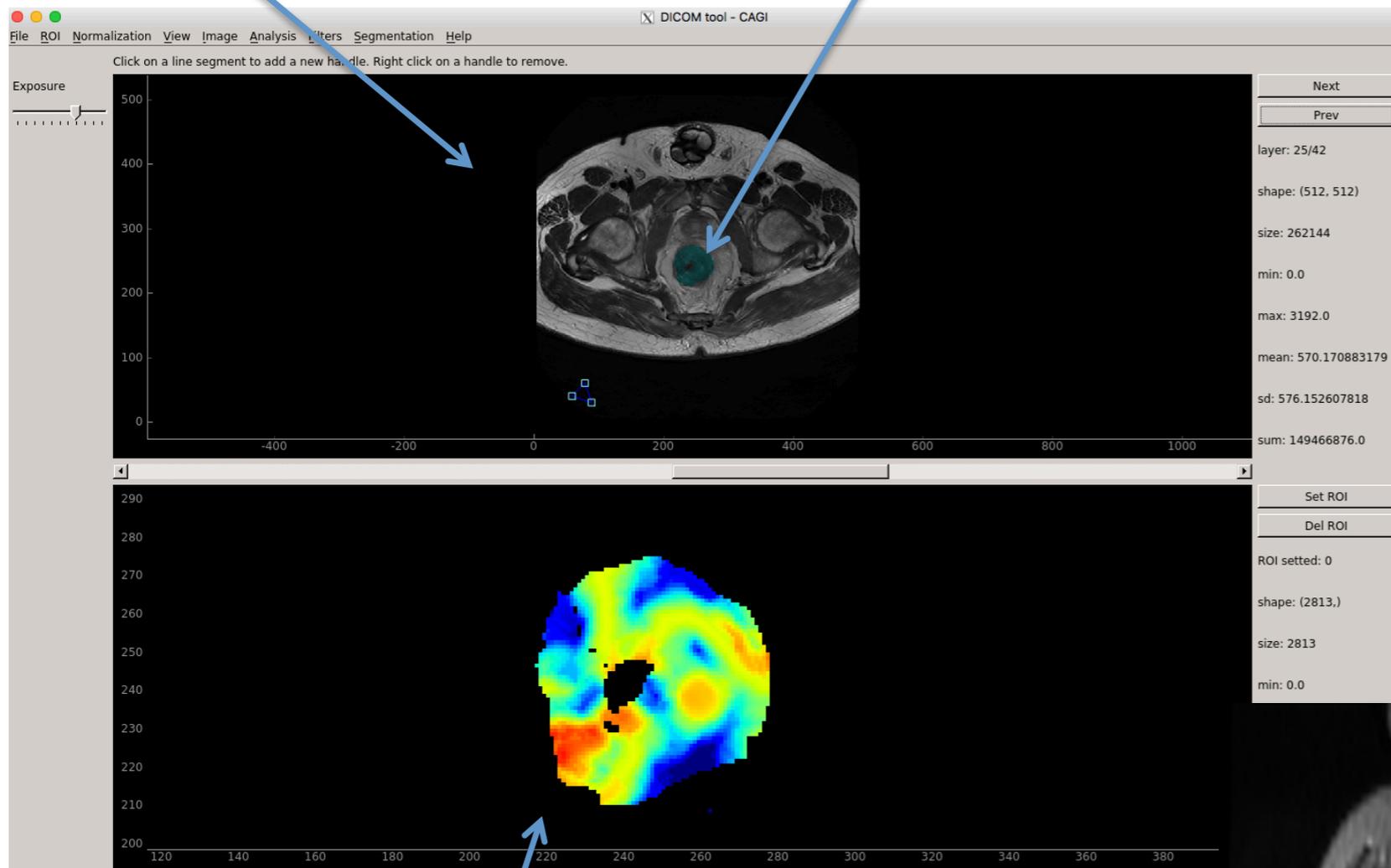
- We developed a custom open-source package in python  
[https://github.com/carlomt/dicom\\_tools](https://github.com/carlomt/dicom_tools)  
<https://pypi.org/project/dicom-tools/>
- The software is able to:
  - read and visualize images in dicom format - import and visualize ROI
  - draw new ROIs
  - allows grey-level intensity normalization (histogram matching and to a pre-defined ROI)
  - implements image filters
  - implements segmentation tools
  - implements texture analysis

# dicom\_tool

T2w slice

Region of interest (ROI) selected by hand by radiologists

Laplacian of Gaussian filter



local Shannon entropy

# dicom\_tool

The screenshot displays the DICOM tool application interface. The main window, titled "DICOM tool - ANFR", features a central image viewer showing an axial MRI scan of a human torso. A teal-colored region of interest (ROI) is highlighted on the scan. To the left of the image viewer is a vertical slider labeled "Exposure" with a white triangle indicating the current level. Below the image viewer is a horizontal scrollbar. To the right of the image viewer is a panel with several buttons: "Next", "Prev", "Set ROI", and "Del ROI". Below these buttons is a list of statistics for the ROI: layer: 22/31, shape: (512, 512), size: 262144, min: 0.0, max: 3254.0, mean: 567.6141586303711, sd: 502.80333555297534, and sum: 154038526.0. Below the main window is a terminal window showing the interactive shell. The terminal output includes the following text:

```
dicom_tool interactive shell.  
  
The dicom_tool application instance is called 'instance'  
so you can access its data members via 'instance.data'.  
If you loaded dicom files the content is stored in 'instance.data',  
the ROI in 'instance.ROI'.  
  
Python 3.6.5 (default, May 18 2018, 18:13:15)  
Type "copyright", "credits" or "license" for more information.  
  
IPython 5.7.0 -- An enhanced Interactive Python.  
?      -> Introduction and overview of IPython's features.  
%quickref -> Quick reference.  
help    -> Python's own help system.  
object? -> Details about 'object', use 'object??' for extra details.  
  
In [2]: instance.goToLayerWithLargerROI()  
  
In [3]: type(instance.data[22])  
Out[3]: numpy.ndarray  
  
In [4]:
```

It allows to open a python interactive shell from which you can call methods and have full access to memory

# ROOT interface

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- dicom\_tools can also export analysis results in ROOT
- A modular scientific software framework
- The most used in High Energy Physics
- Developed at CERN
- It provides all the functionalities needed to deal with big data processing, statistical analysis, visualisation and storage.
- Open-source
- Mainly written in C++ but integrated with other languages such as Python and R



<https://root.cern.ch/>

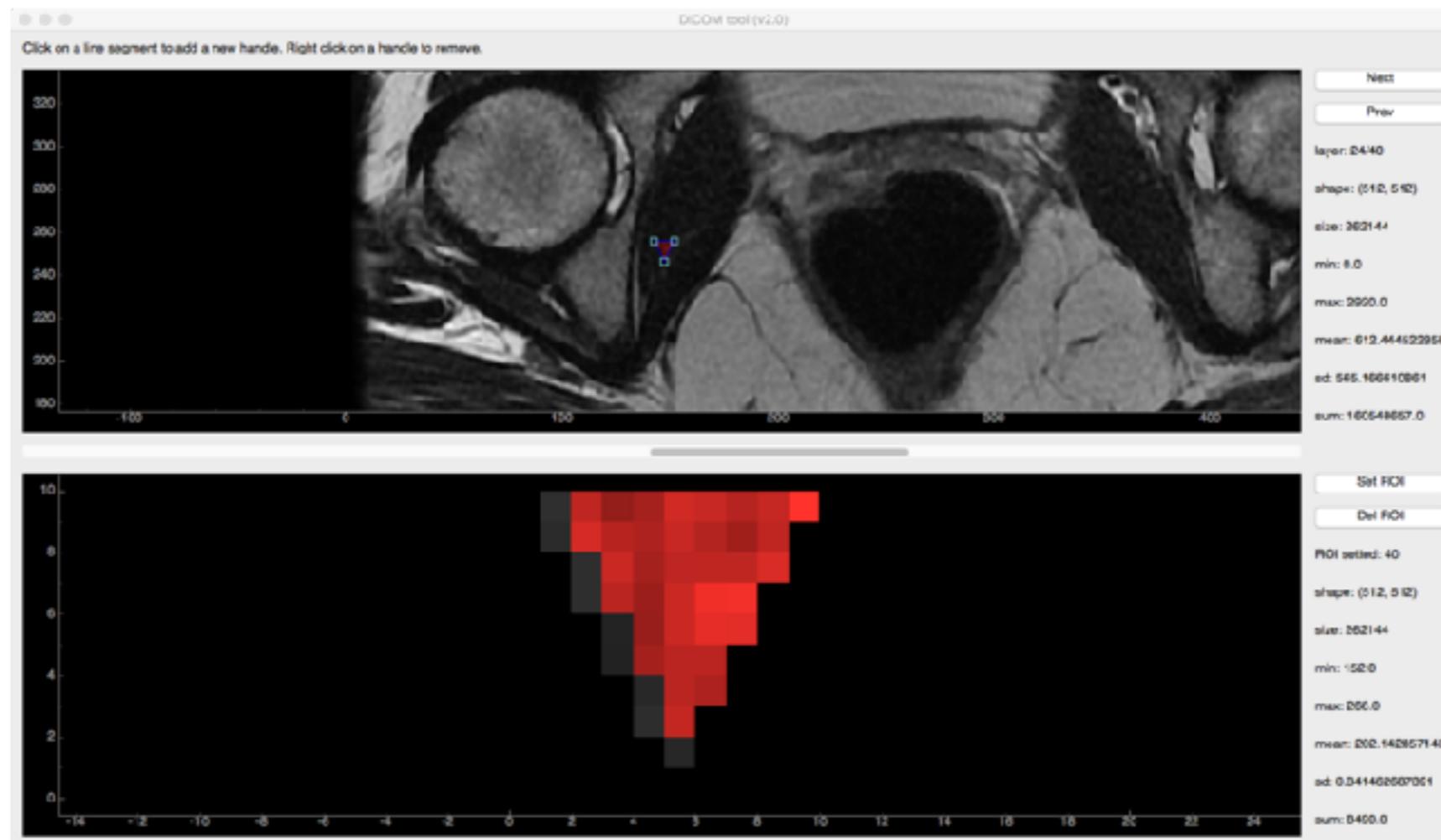
# Normalization

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- Intensity in MRI has not an immediate physical meaning (unlike Hounsfield units in CT)
- This affects data analysis that rely on intensity
- To compare outputs from different machines/centers
- But also to compare two different images during the same acquisition (i.e.: same patient)
- A calibration would be useful

# Normalization to the muscle

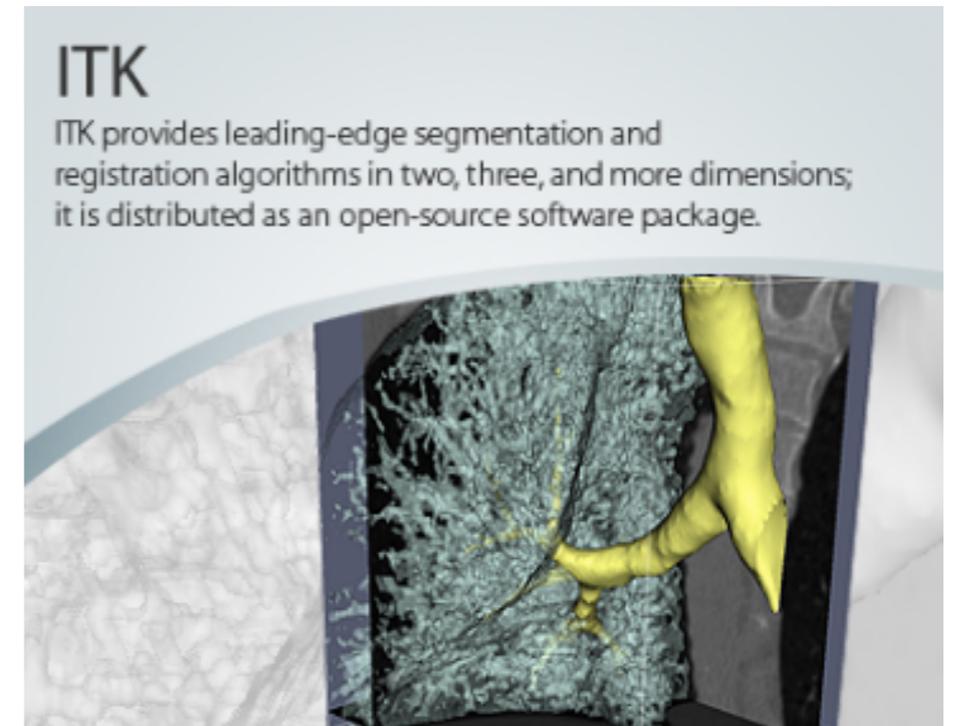
- Manually select a "normalization" ROI for each slice
- Only one point...



# ITK Interface

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- Dicom\_tools is interfaced with:  
**Insight Segmentation and Registration Toolkit (ITK)**
- It is an open-source, cross-platform system that provides developers with an extensive suite of software tools for image analysis
- Developed through extreme programming methodologies, it employs leading-edge algorithms for registering and segmenting multidimensional data

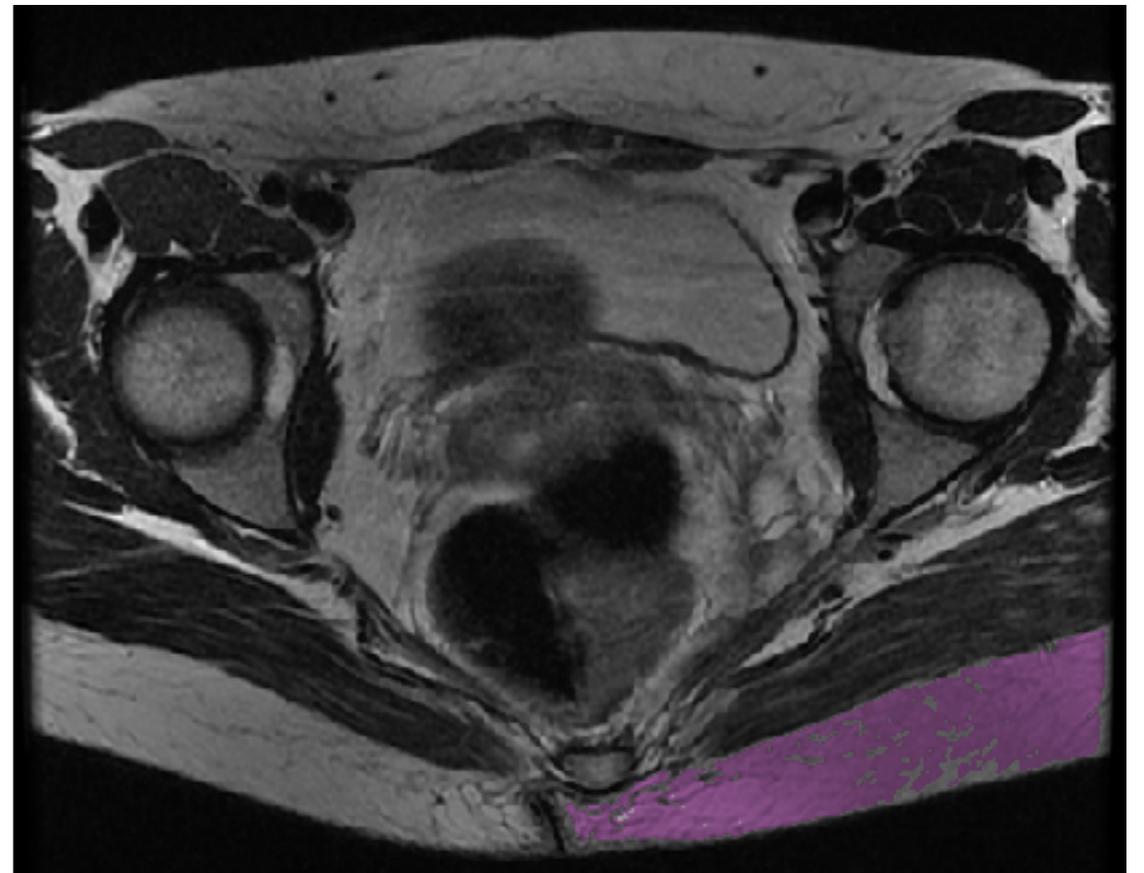


<https://itk.org/>

# Connected threshold

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- A Region Growing algorithm
  - Starts from a seed point
  - pixels in the neighbourhood are evaluated to determine if they are part of the object
  - If so, they are added to the region and the process continues as long as new pixels are added to the region
- Connected threshold includes pixels in the growing region if inside a given intensity interval



# Morphological Watersheds

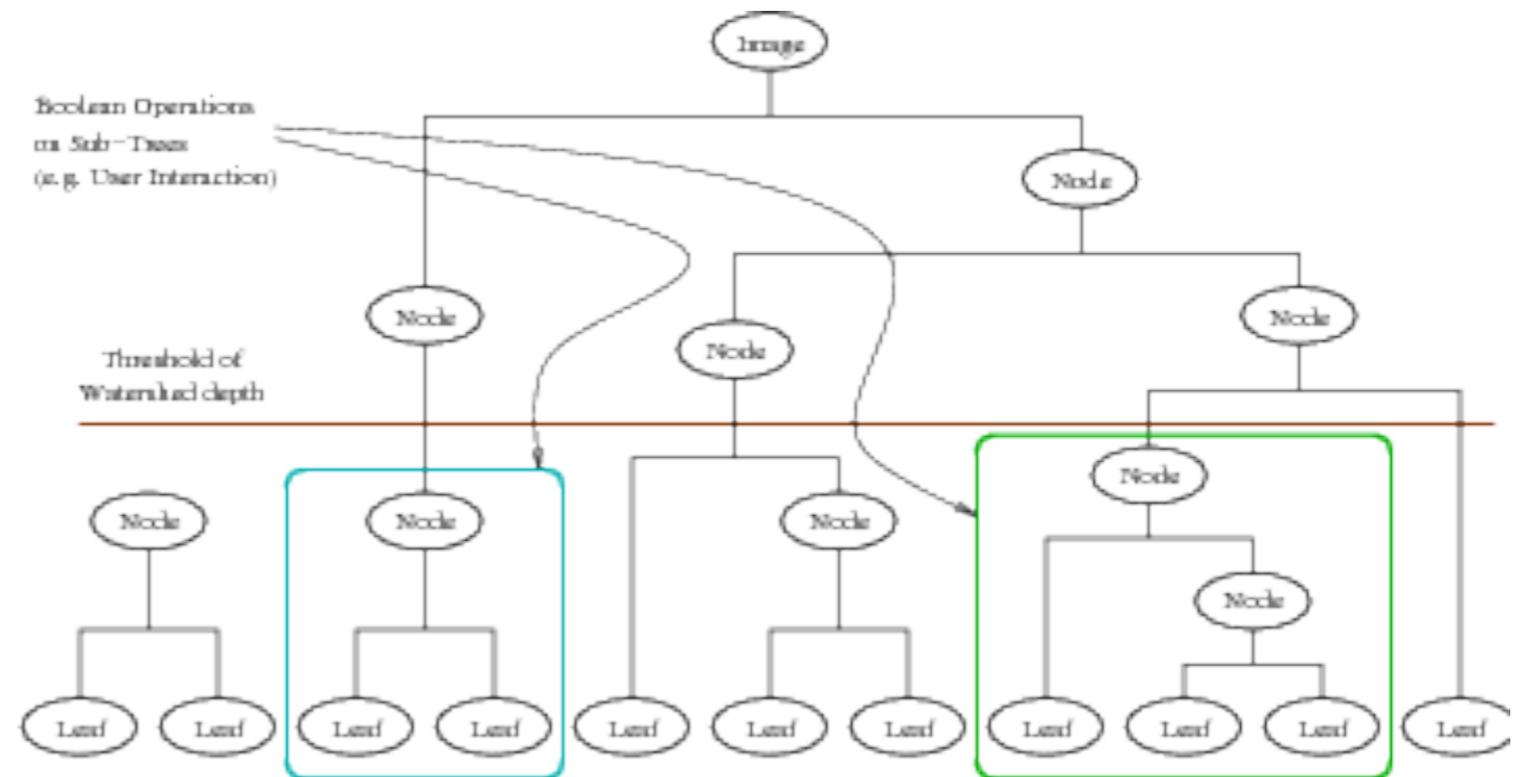
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- Classifies pixels into regions using gradient
- it produces a region for each local minimum
- to alleviate the over-segmentation, it is possible to define a minimum watershed depth
- the watershed depth is the difference in height between the minimum and the lowest boundary point



# Morphological Watersheds

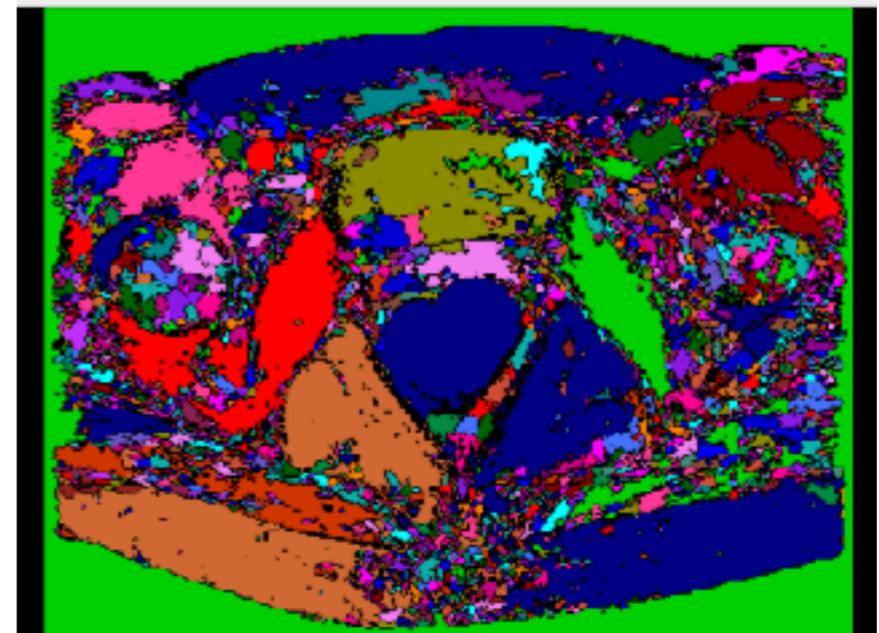
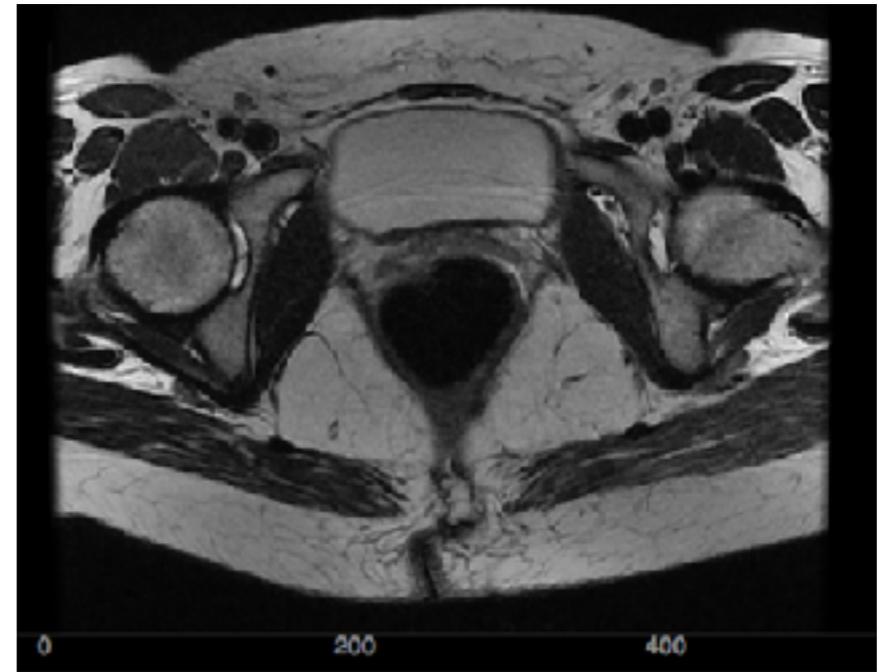
- This technique is less sensitive to user-defined thresholds than classic region-growing methods
- may be better suited for fusing different types of features from different data sets
- it produces hierarchy of segmentations from which a single region or set of regions can be extracted a-priori, using a threshold, or interactively, with the help of a graphical user interface



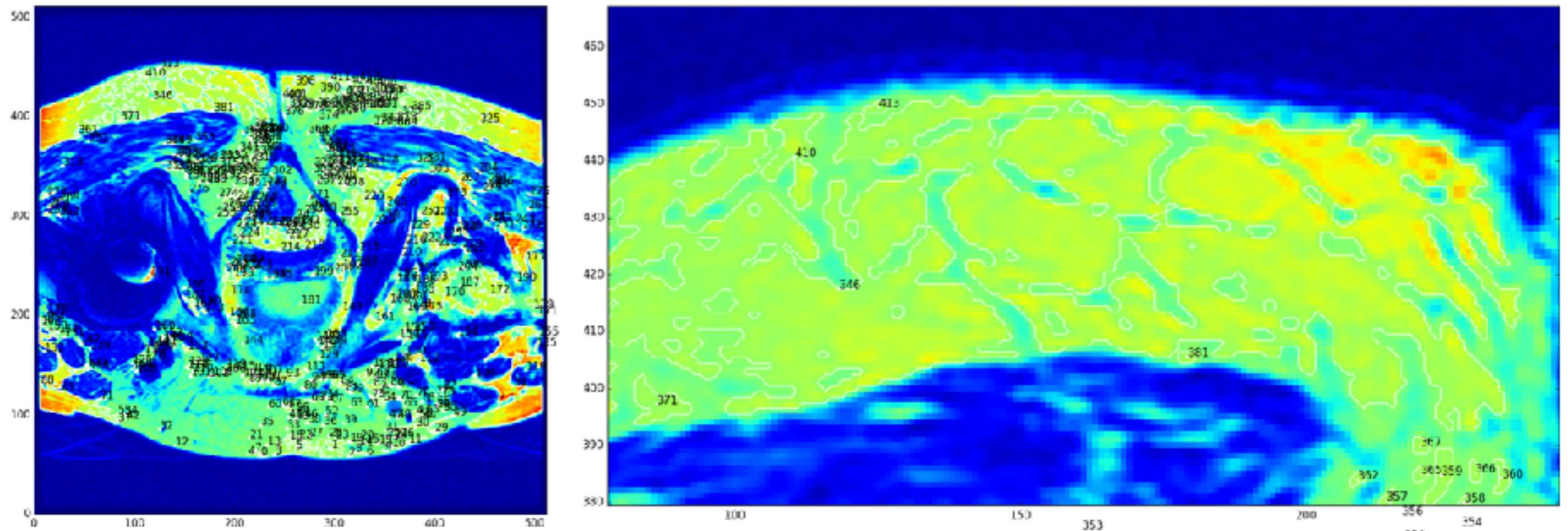
# Morphological Watersheds

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- Preliminary results are encouraging
- We have to optimize all the parameters
- 3D segmentation



# Segmentation with Asterism

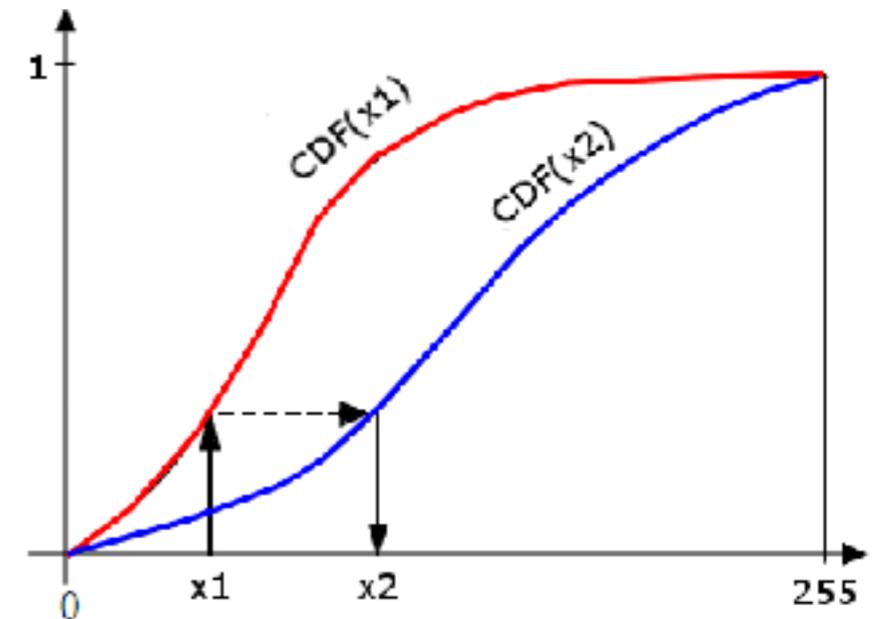


- Asterism is a python tool developed by Andrea Tramacere (Observatory of Geneva)
- made for finding clusters in astrophysical images (Fermi)

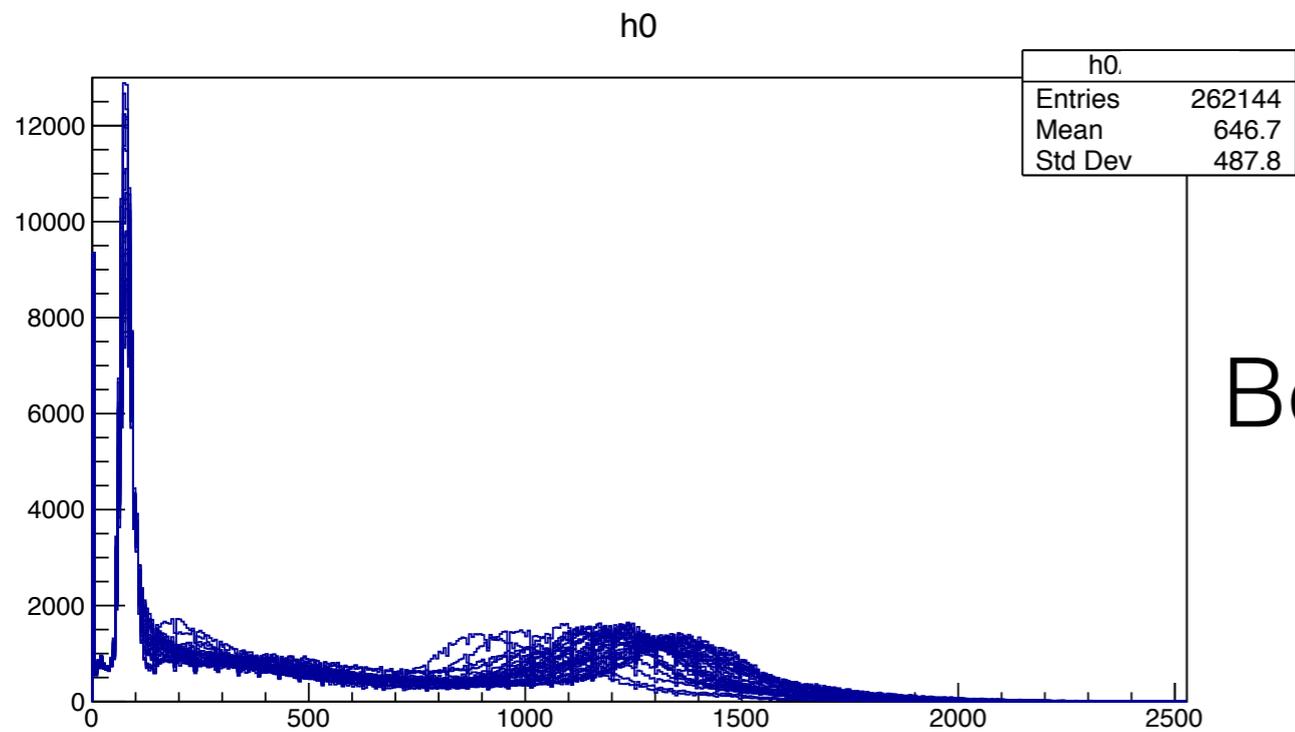
# Histogram matching

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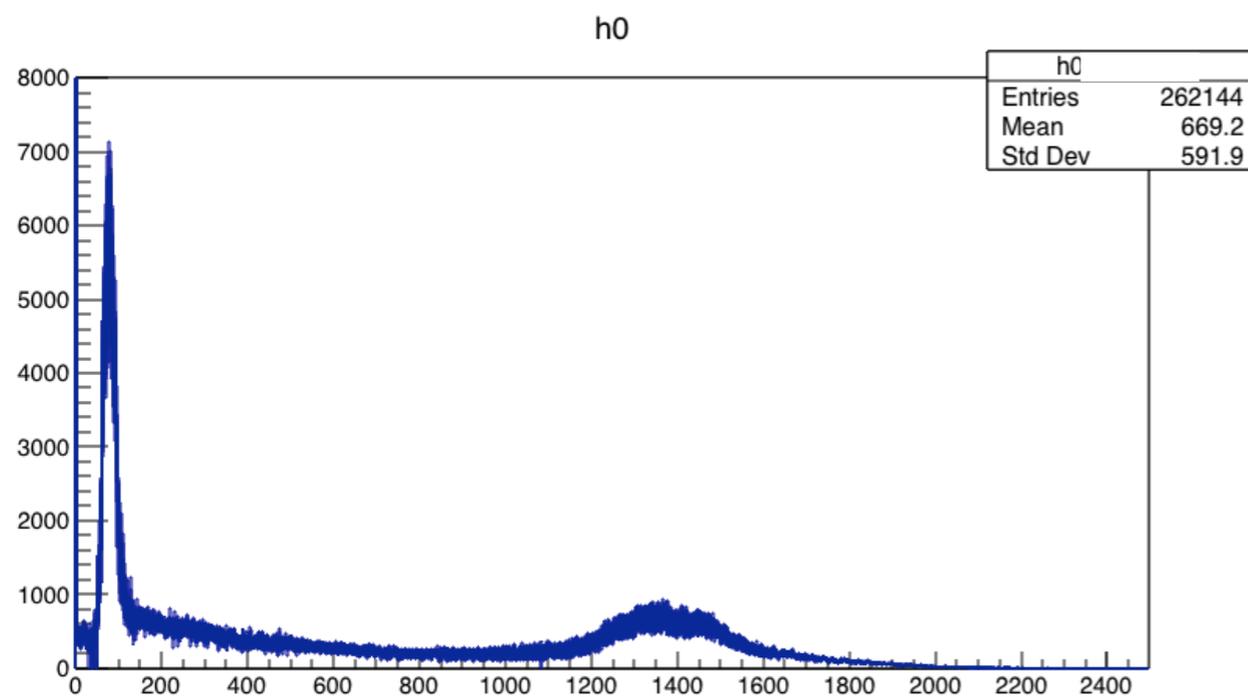
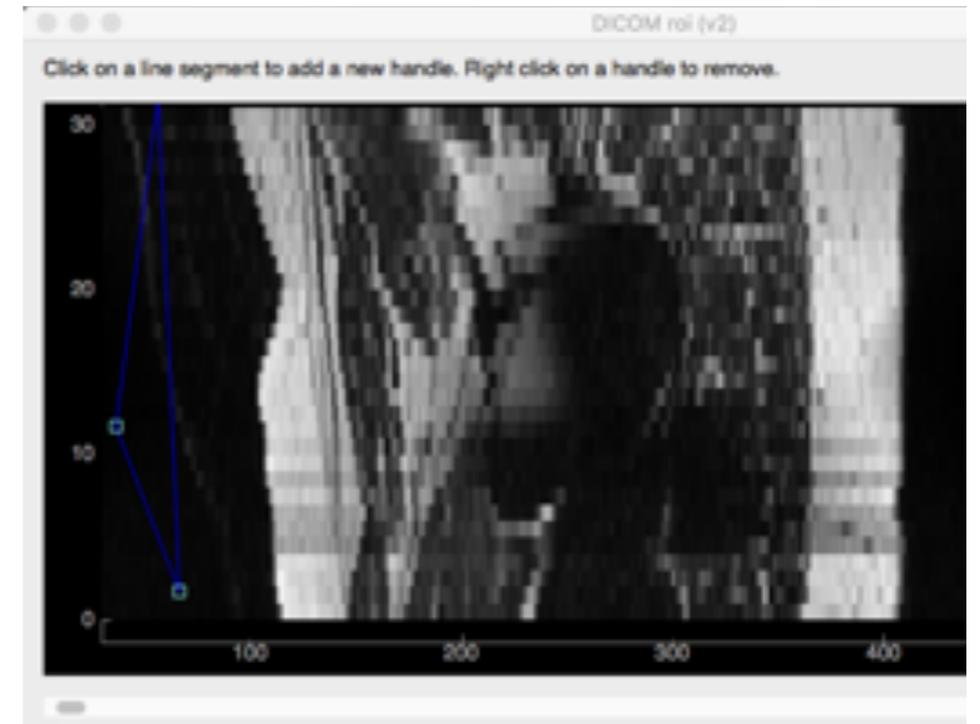
- One image is used as template
- It assumes the same amount of pixel per region in the image and in the template
- Recognizes regions using the cumulative distribution of the image and the template
- Assigns the same region color to the image pixels as the template



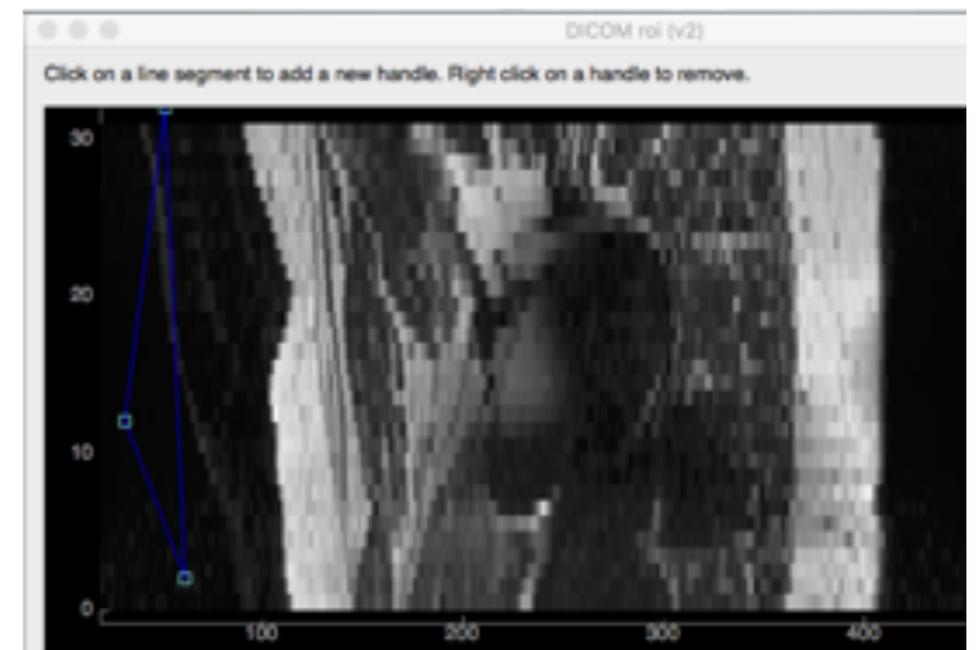
# Results of Histogram Matching



Before

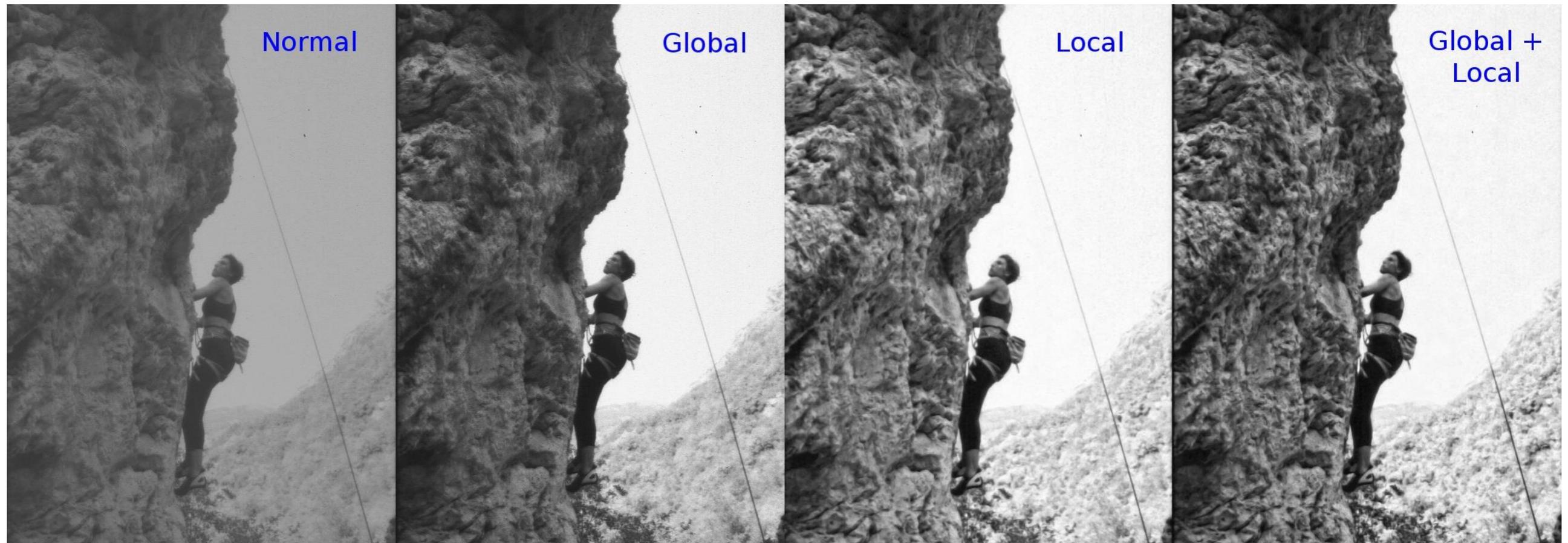


After



# Contrast Limited Adaptive Histogram Equalization

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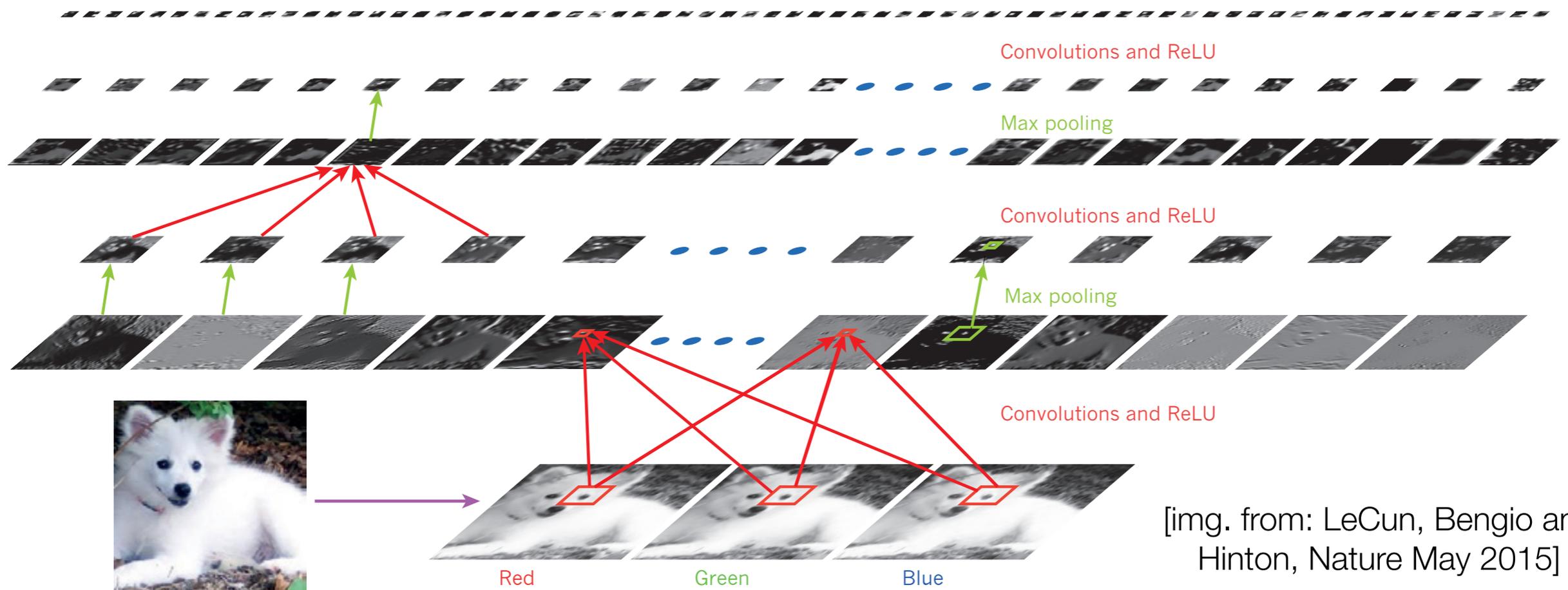


- Histogram equalization for each section of the image
- Contrast amplification is limited to avoid noise amplification

# Deep Learning

# Deep Learning

- Each rectangular image is a feature map
- A score is computed for each image class in output
- ReLU = rectified linear unit



# Segmentation

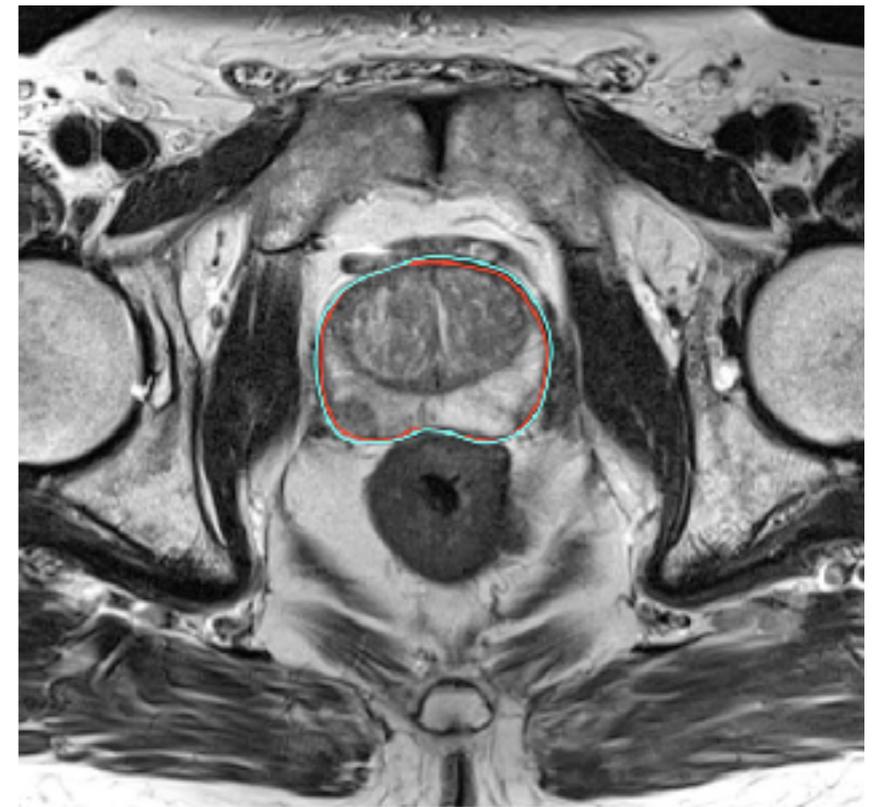
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- Identify a portion of an image given the context
- Many deep learning applications are about object recognition
- Simple task for a humans but hard for algorithms
- Challenge:
  - Small dataset

# ProMISe Challenge

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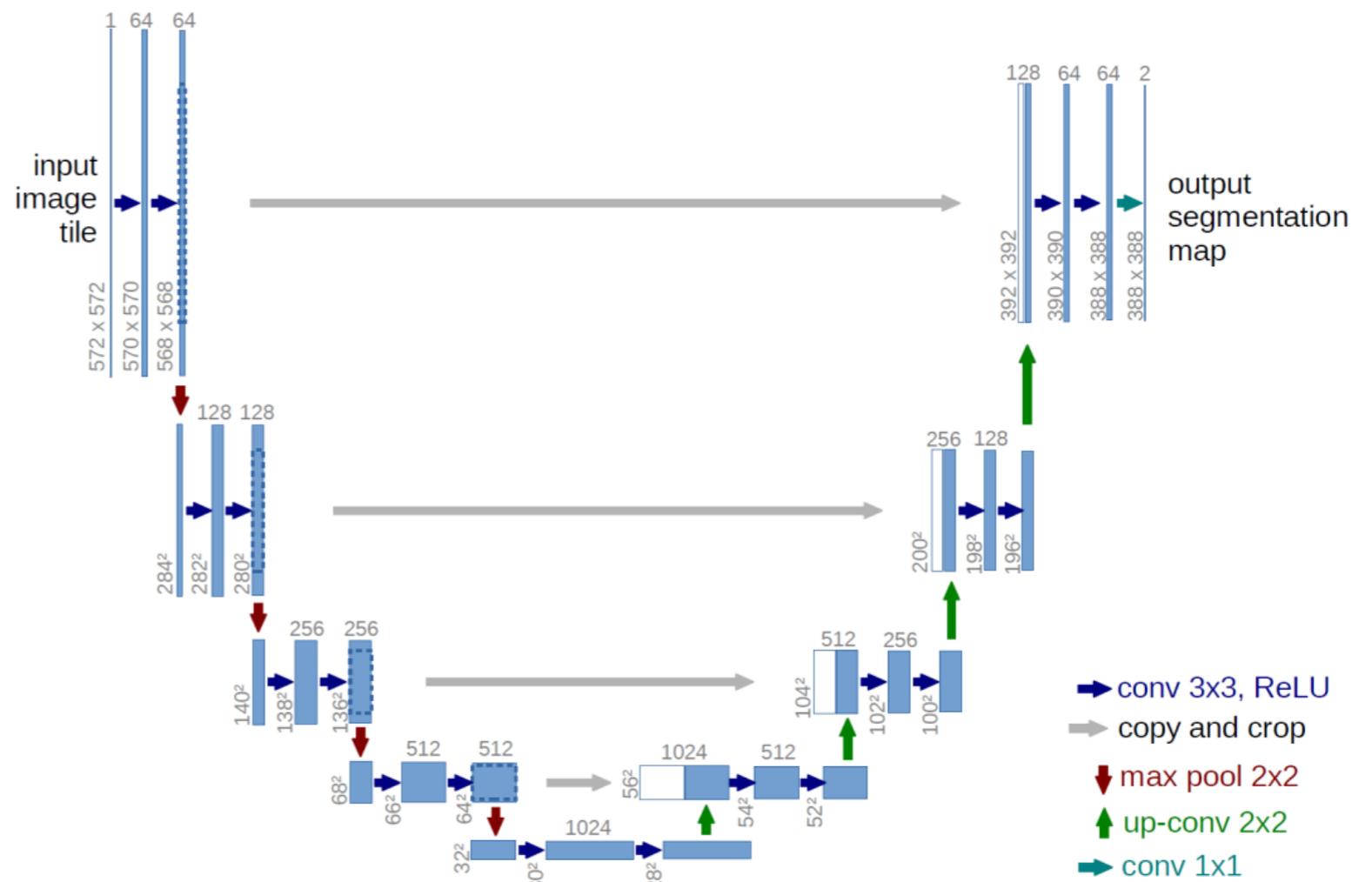
- Prostate MR Image Segmentation 2012
- The data includes both patients with benign prostatic hyperplasia and prostate cancer.
- The data includes both patients with benign prostatic hyperplasia and prostate cancer.
- 50 cases (about 500 usable slices)
- Reference segmentation included



<https://promise12.grand-challenge.org>

# U-net

- developed for biomedical image segmentation
- fully convolutional network
- consists of a contracting path and an expansive path



[img. from: Ronneberger et. al. arXiv:1505.04597v1]

# Data augmentation

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- Essential to teach the network the desired invariance and robustness properties
- Especially when few training samples are available
- Shift and rotation
- Deformations and intensity variations
- Random elastic deformations

# A convolutional block

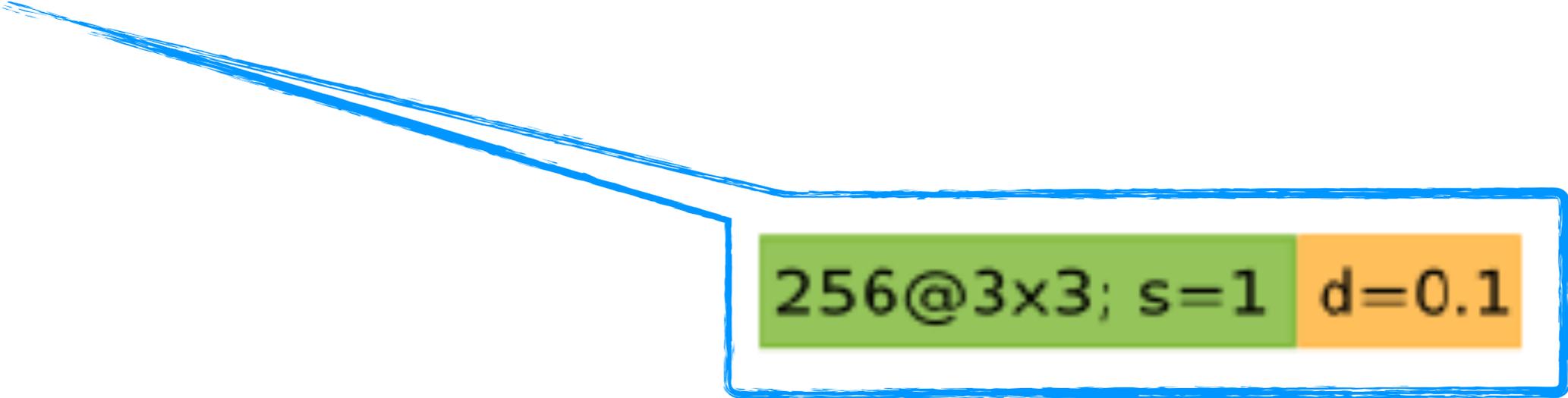
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256@3x3; s=1 d=0.1

# A convolutional block

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- One of more convolutional layers

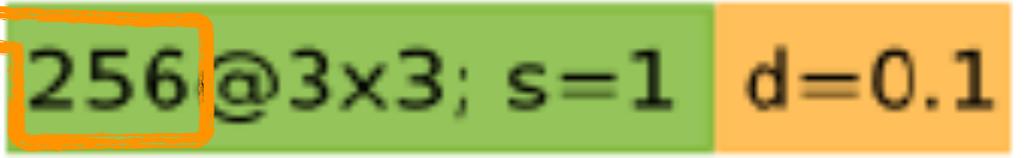


256@3x3; s=1 d=0.1

# A convolutional block

---

- One of more convolutional layers
- Number of features



256 @ 3x3; s=1 d=0.1

The diagram shows a horizontal bar divided into two colored sections. The left section is green and contains the text '256 @ 3x3; s=1'. The right section is orange and contains the text 'd=0.1'. An orange arrow points from the text 'Number of features' in the list above to the '256' in the green section.

# A convolutional block

---

- One of more convolutional layers
- Number of features
- Kernel dimension

256@3x3 s=1 d=0.1



# A convolutional block

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- One of more convolutional layers
- Number of features
- Kernel dimension
- Stride

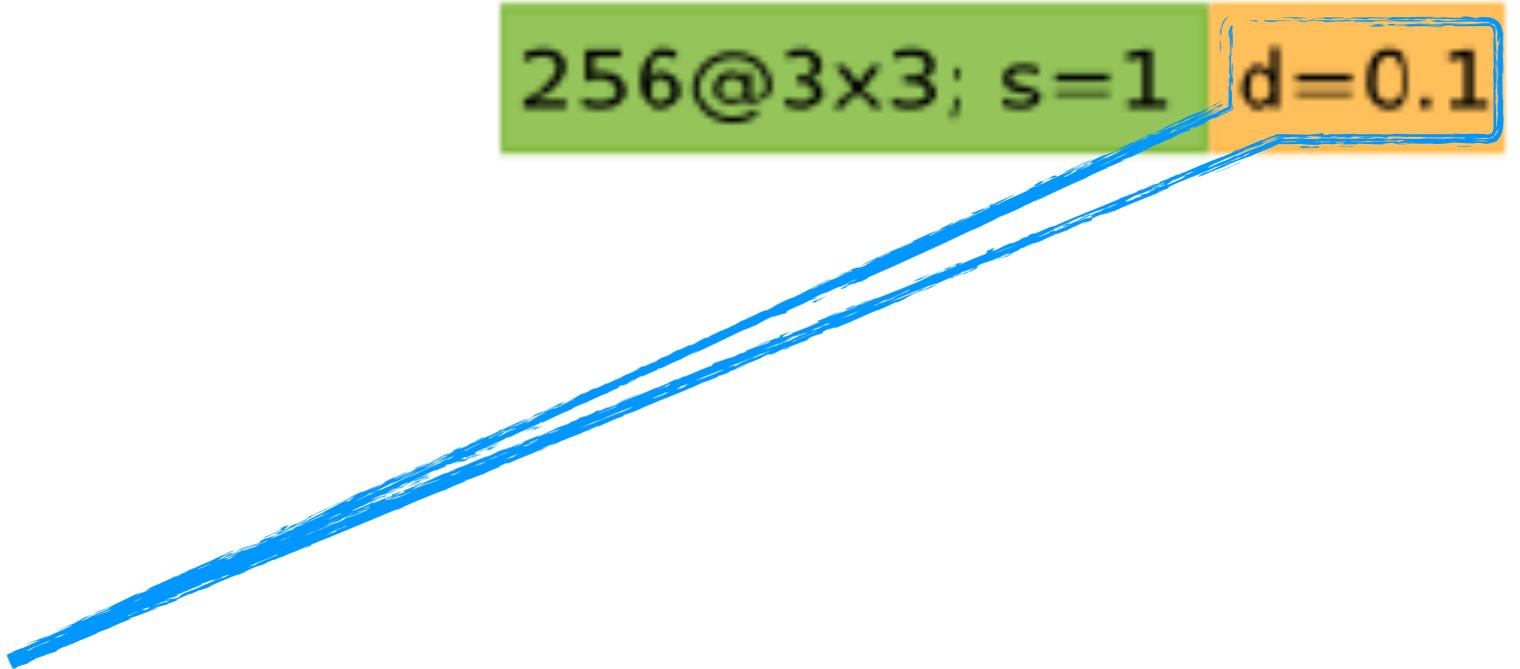
256@3x3: s=1 d=0.1

# A convolutional block

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- One of more convolutional layers
- Number of features
- Kernel dimension
- Stride
- Drop-out probability

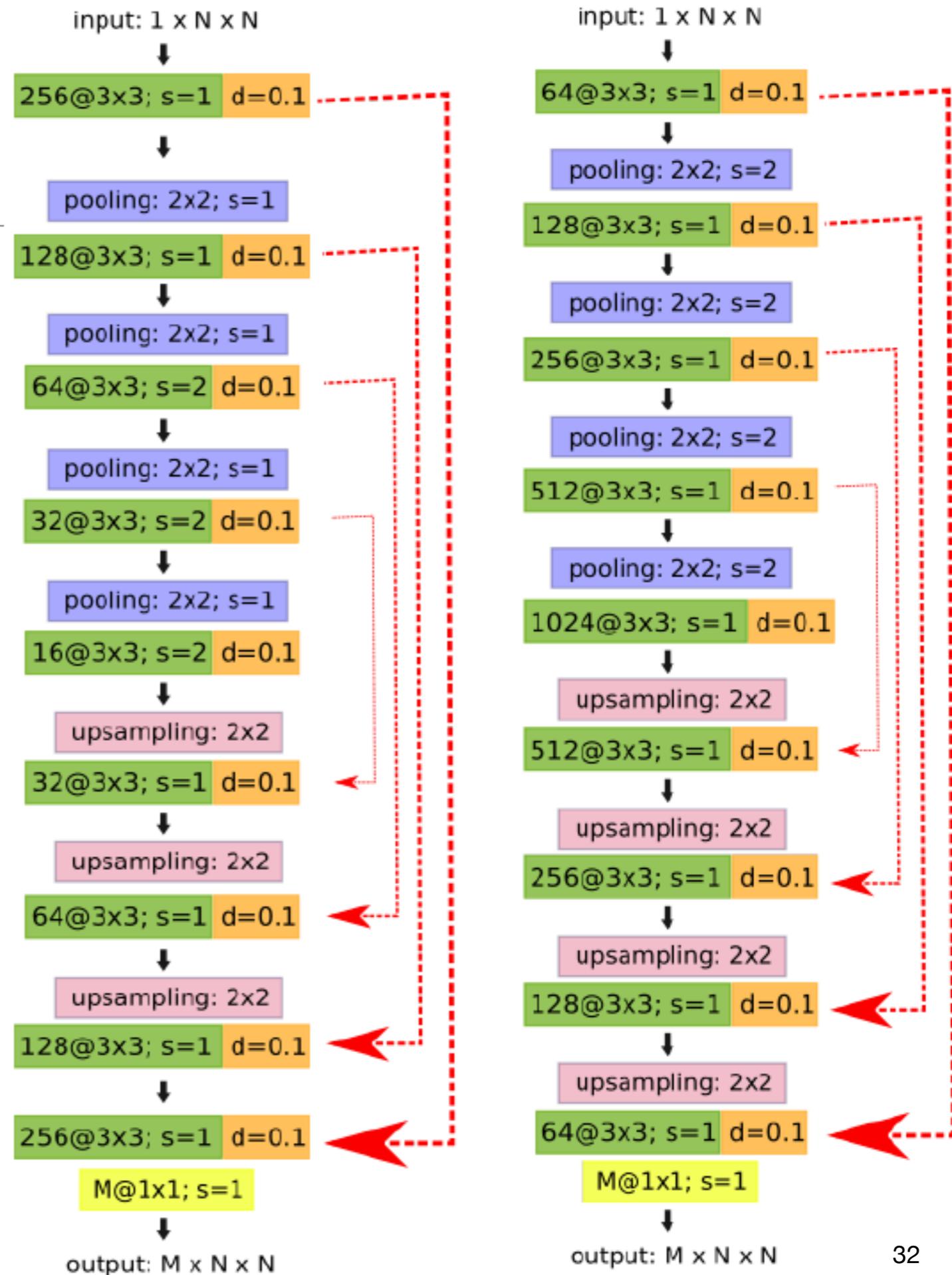
256@3x3; s=1 d=0.1



# Modifications of U-net

- All Drop-Out
- 30 M parameters
- dropout after every convolutional
- InvertedNet
- less parameters
- 1.4 M parameters

[img. from: A.Novikov et al.  
arXiv:1701.08816v4]



# Cost function and its optimization

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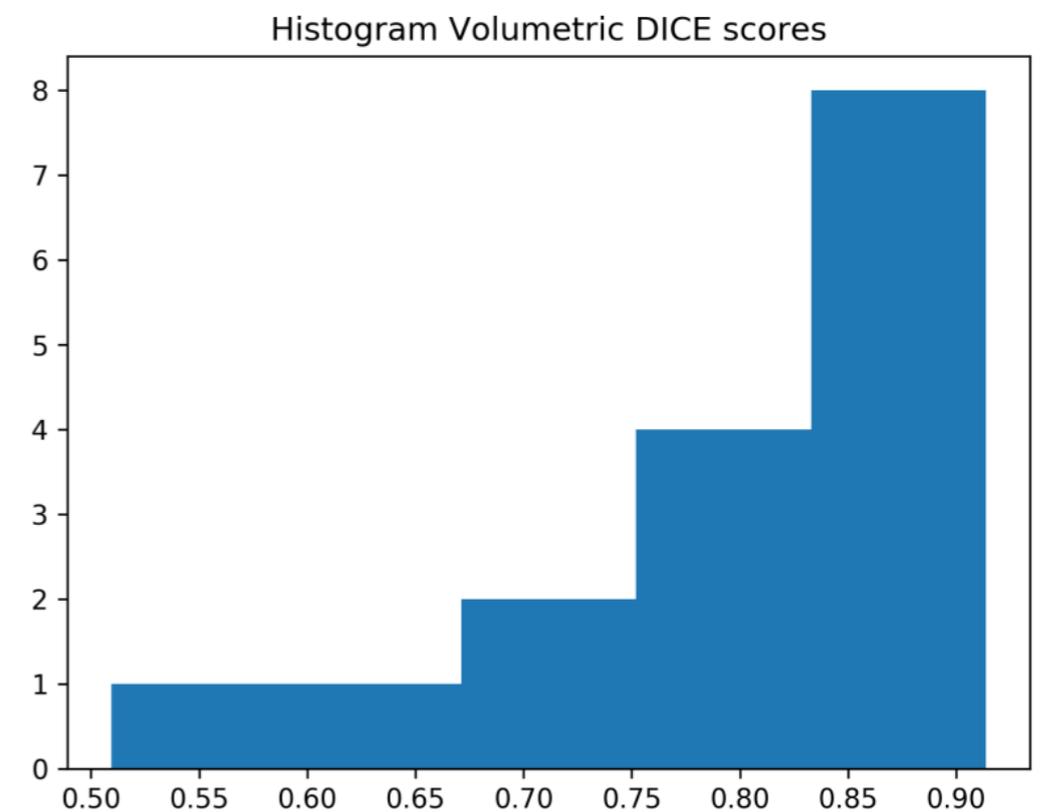
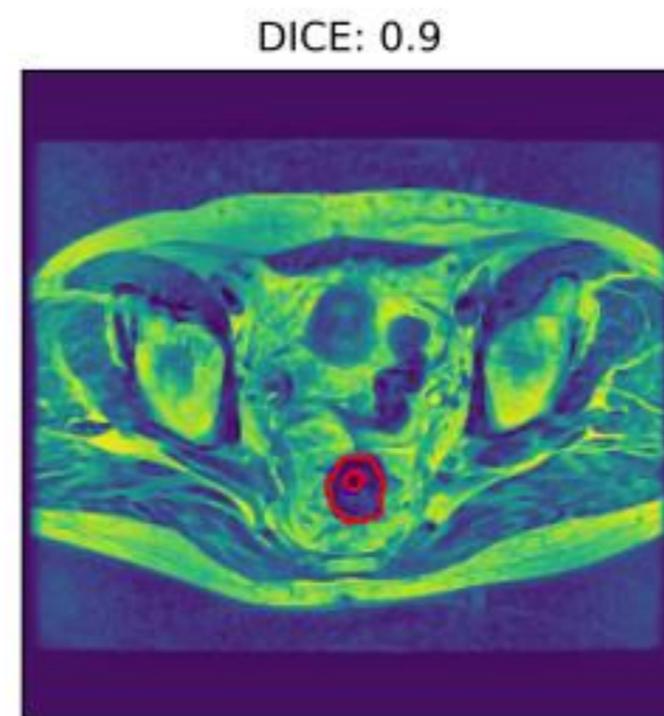
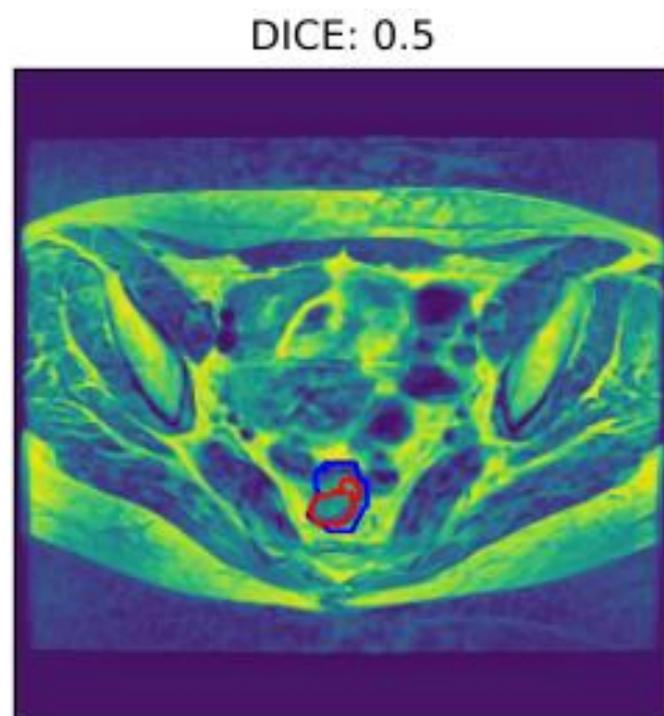
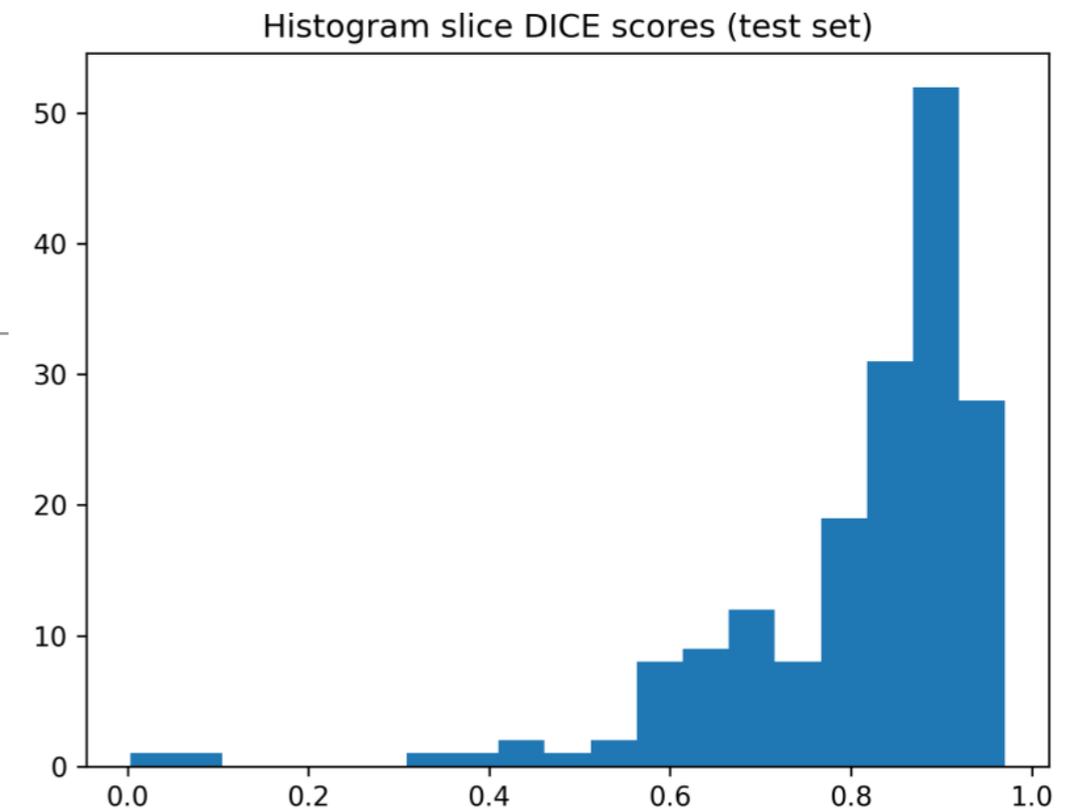
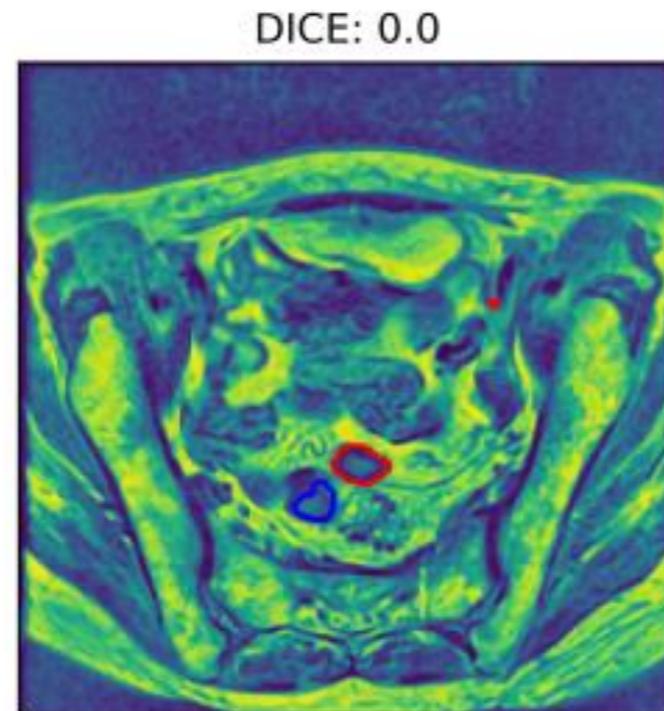
- Dice's coefficient (or Sørensen index, or also similarity coefficient) is for estimating the similarity of two samples
- It equals twice the number of elements common to both sets divided by the sum of the number of elements in each set:

$$C_{Dice} = 2 \frac{\sum_i (x_i \cdot \chi_i) + \epsilon}{\sum_i (x_i + \chi_i) + \epsilon}$$

- Optimized using Adam (Adaptive Moment estimation), a stochastic gradient descent algorithm
- The speed is function of the running averages of the gradients and the second moments of the gradient

# Results - Inverted Net

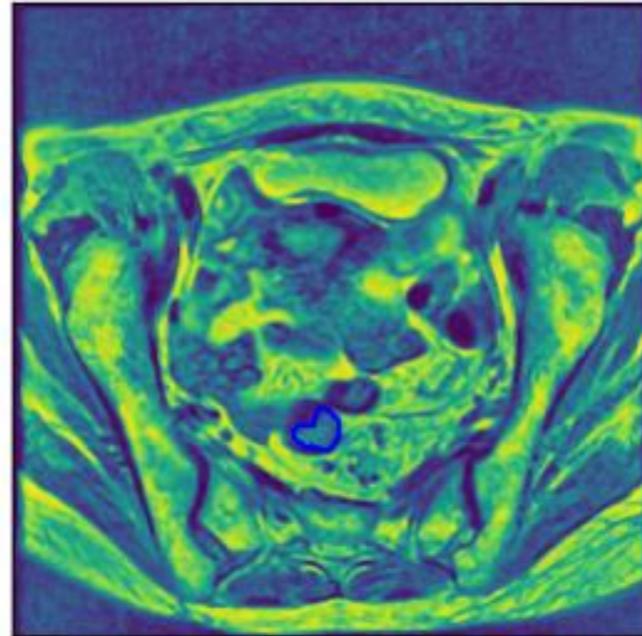
- 1.4 M parameters
- 38 patients for training
- 16 for test



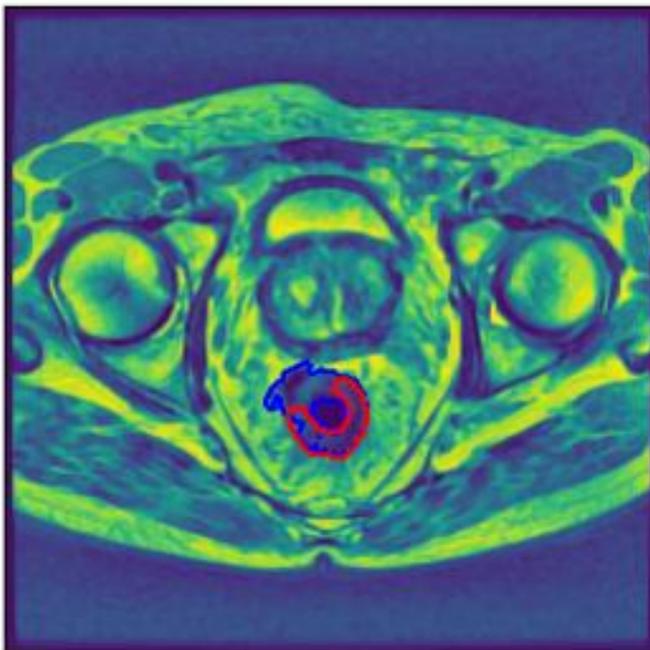
# Results - All Drop-Out

- 30 M parameters
- 4 times slower than InvertedNet

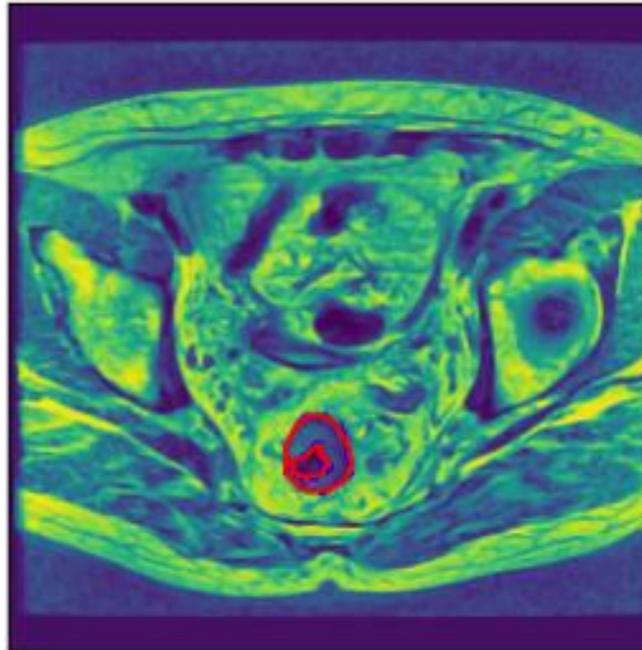
DICE: 0.0



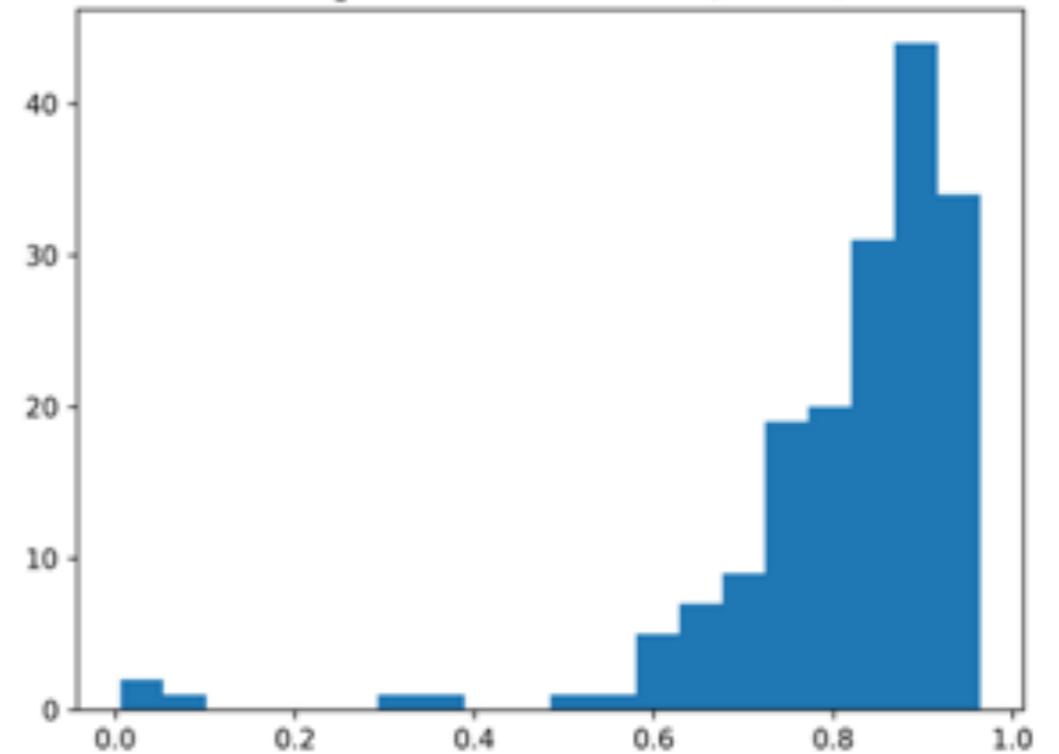
DICE: 0.5



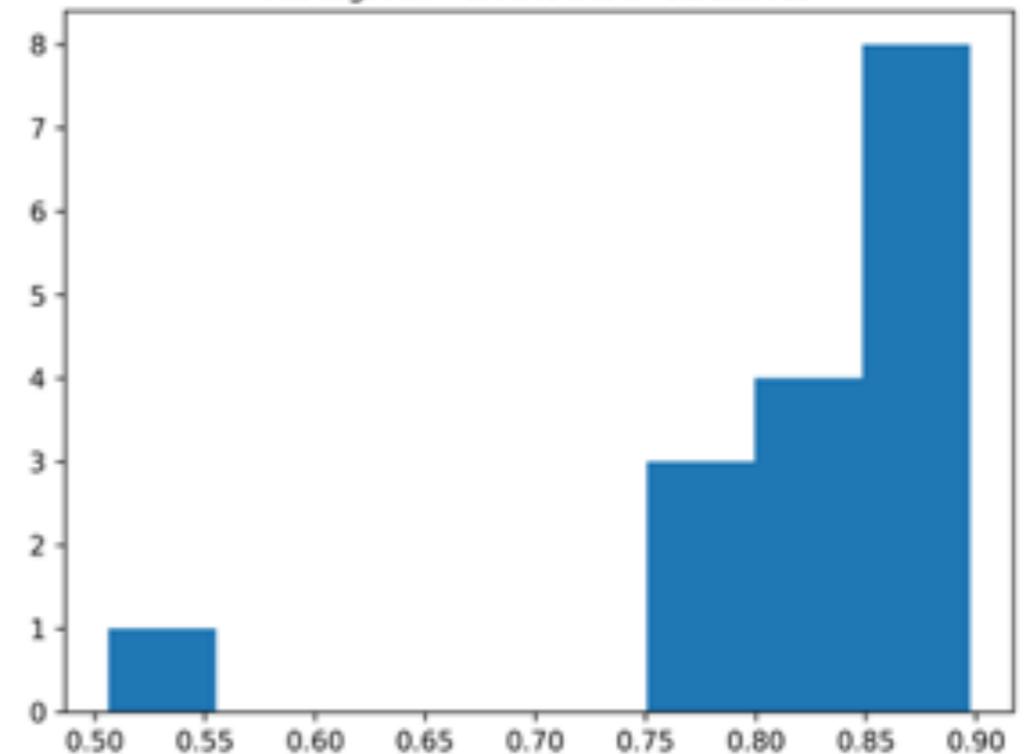
DICE: 0.9



Histogram slice DICE scores (test set)



Histogram Volumetric DICE scores



# Summary

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- MR Images could be analysed to find features not-visible even to trained Medical Doctors
- We developed a tool to import images converting them to 3D numerical tensors
- It allows to pre-process the data and compute texture parameters
- We started to apply Deep Learning algorithms

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*thank you for your attention!*