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iBiopsy

non-invasive, deep-learning diagnostic tools for prostate and liver disease

Data Science Meetup
May 16, 2018

Who is Median Technologies?

Transforming the science of medical imaging

Our Beginning: Pioneering the industry – extracting the most meaning out of medical images since 2002

Our Business: Best-in-class technology, including artificial intelligence, leverages the power of *Imaging Phenomics®* to improve current treatments, enhance diagnostics and accelerate the development of next generation therapies

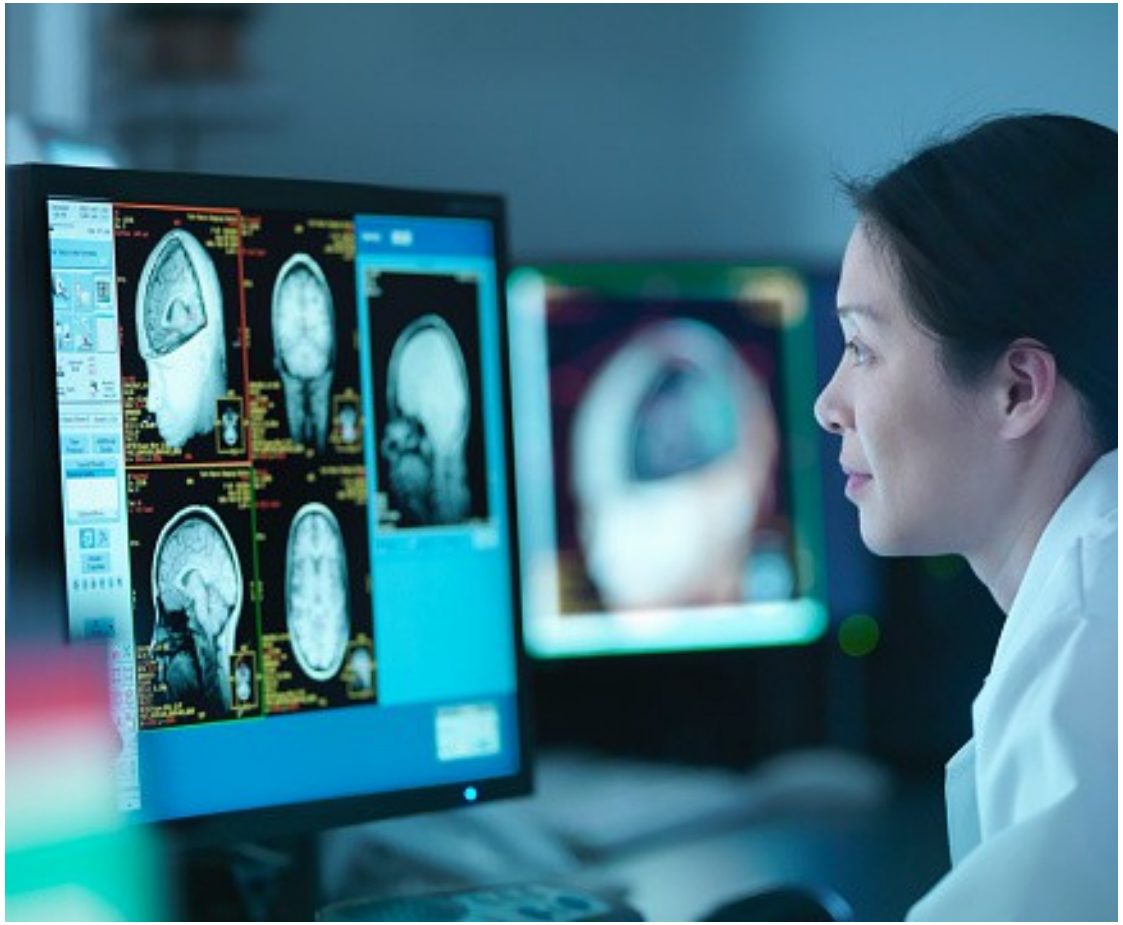
Our Growth: Powered by proprietary technology, robust Key Opinion Leader (KOLs) connections and strong partnerships and collaborations

Our People: >140 employees worldwide with offices in France, U.S.A. and China

Our Vision: Leverage medical imaging to enable precision medicine and accelerate the development of new, innovative technologies and treatments for patients who need them

The Transformative Power of Imaging

Unlock the potential of personalized medicine



Cancer

Continues to be one of the top 2 causes of death.

>600M

Imaging procedures per year the U.S. with most having an AI post-processing component in the future.

Rise in -omics

Need approach to capitalize on phenomics, genomics and big data

20%

Most new immuno-oncology treatments only have about 20% responders. Treatment response assessment with imaging will improve personalized treatment.

Artificial Intelligence

Matches disease characteristics to histopathology outcome to drive success.

Personalized Medicine

Personalized prevention and treatment will rely on imaging data in addition to genomic data.

Industry-leading Partnerships

Working with thought-leaders and top innovators in healthcare

Clinical Trials

Global Contract Research Organizations (CROs)

medidata

Syneos Health

START "The cure starts here."

Patient Care

Top hospital systems around the globe

Memorial Sloan Kettering Cancer Center

Centre Hospitalier Universitaire de Nice

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Tools & Diagnostics

Technology Research Partners and Pharma/Healthcare

Top 10 Pharma

Canon

Inria INVENTEURS DU MONDE NUMÉRIQUE

Market-based collaborations with top pharma, CROs and hospitals

** Not an exhaustive partnership listing*

Talk Overview

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Medical Imaging & Deep Learning

iBiopsy® for *Prostate*

iBiopsy® for *Liver*

Encryption For Medical Imaging

Overview of Medical Imaging & Deep Learning Methods

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Medical Imaging

The beginnings

VOL. 81 NO. 2

Radiology

AUGUST 1963

a monthly journal devoted to clinical radiology and allied sciences

PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, INC.

The Coding of Roentgen Images for Computer Analysis as Applied to Lung Cancer[1]

GWILYM S. LODWICK, M.D., THEODORE E. KEATS, M.D., and JOHN P. DORST, M.D.

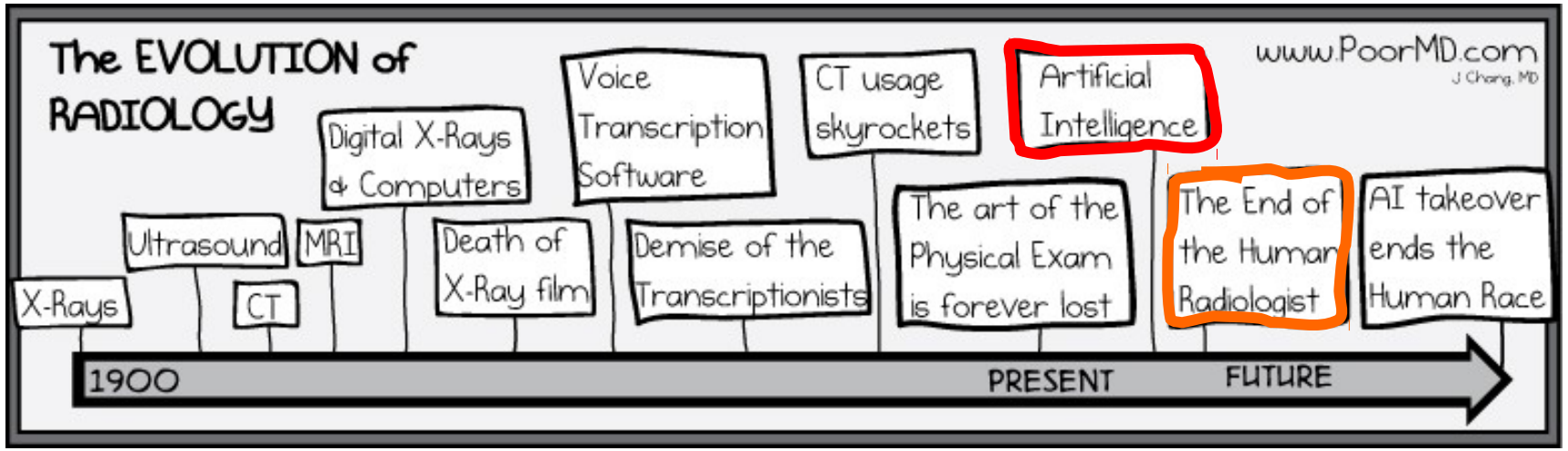
THIS PAPER WILL DESCRIBE a concept of converting the visual images on roentgenograms into numerical sequences that can be manipulated and evaluated by the digital computer and will report the results of employing this system to determine the significance of certain radiographic findings in lung cancer. The development of such a coding system for cause, against a background of air density, the intimate details of the relationship between tumor and host may be faithfully reproduced roentgenographically. Parenthetically, it may be stated that similar density ranges exist in the relationships between bone and soft tissue and that an equally effective descriptive system has been evolved for bone sarcomas (1, 2).

https://pubs.rsna.org/doi/10.1148/81.2.185?url_ver=Z39.88-2003&rfr_id=ori%3Arid%3Acrossref.org&rfr_dat=cr_pub%3Dpubmed

Note of Caution

a.k.a. why the world hates AI researchers

https://www.youtube.com/watch?v=2HMPRXstSvQ



http://www.poormd.com/2016/12/evolution-of-radiology.html

Deep Learning in a Nutshell

From Conventional Machine Learning to Representation Learning

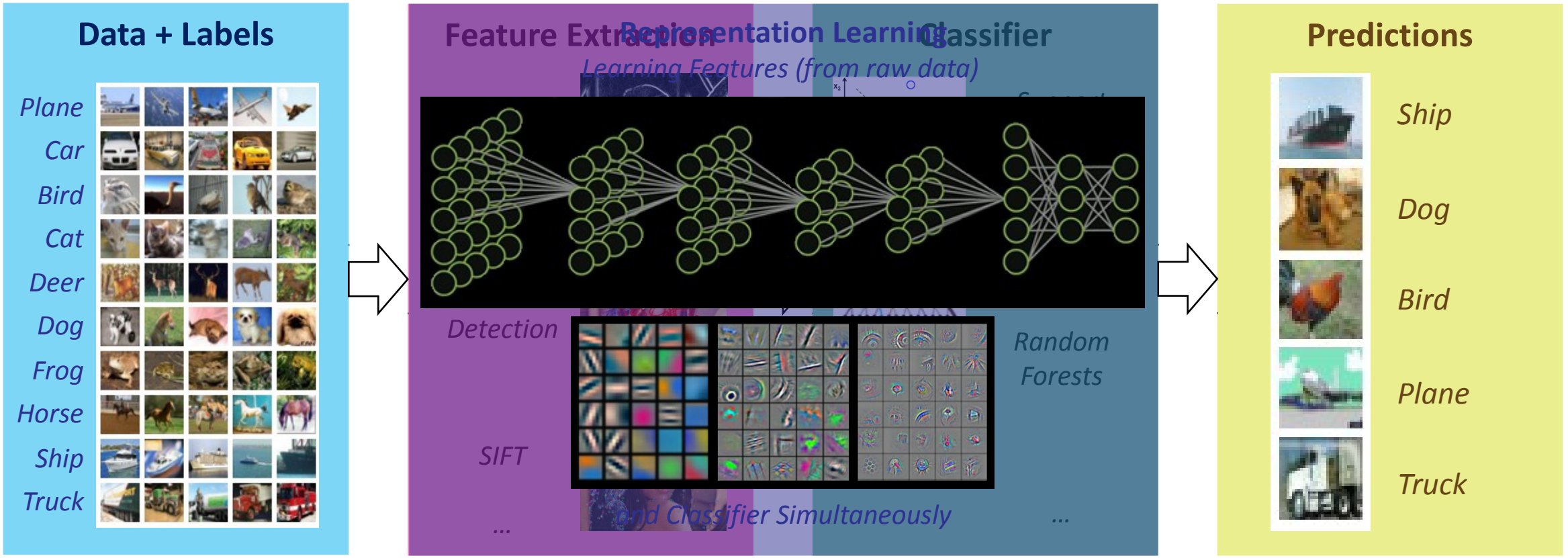
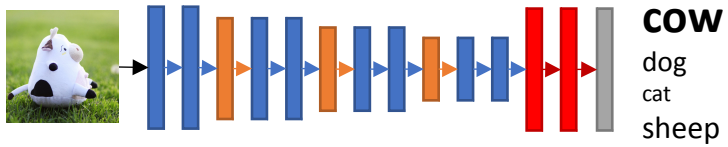


Image Sources: [Lee, Grosse, Ranganath, Ng, 2011] [Zeiler, Fergus, 2013]

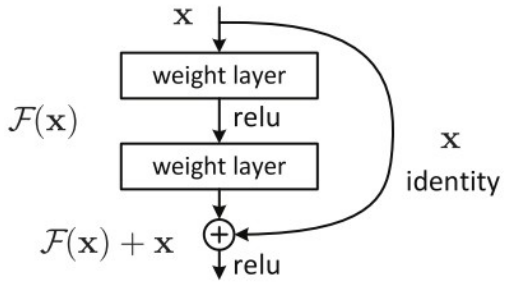
Traditional Architectures

And their building blocks

Classification



$$loss = CategoricalCrossEntropy\ (y, \hat{y})$$

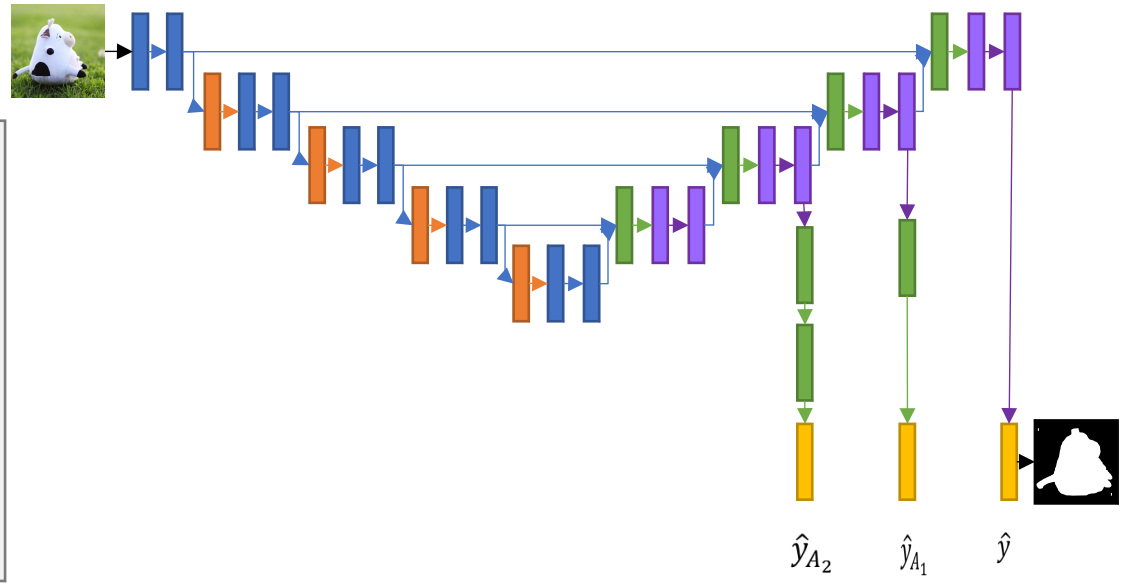


Residual Block

Building Blocks

conv	3x3
pool	2x2
up	2x2
conv	1x1
deconv	3x3
fully connected	
softmax	

Segmentation



$$loss = CrossEntropy\ (y, \hat{y}) \quad + \alpha_1 CE(y, \hat{y}_{A_1}) + \alpha_2 CE(y, \hat{y}_{A_2})$$

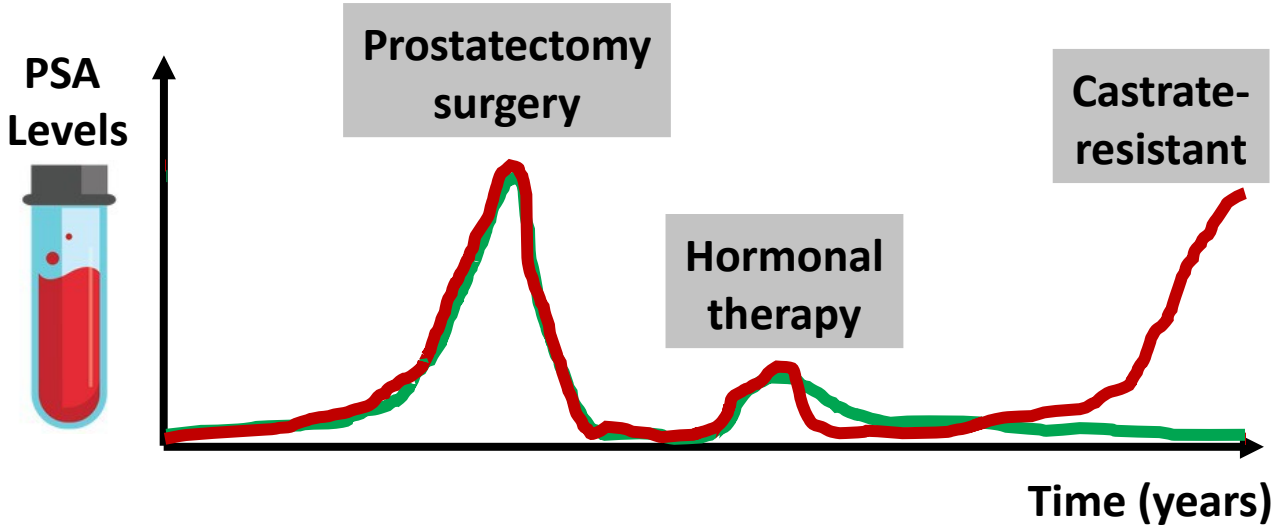
iBiopsy® for *Prostate*

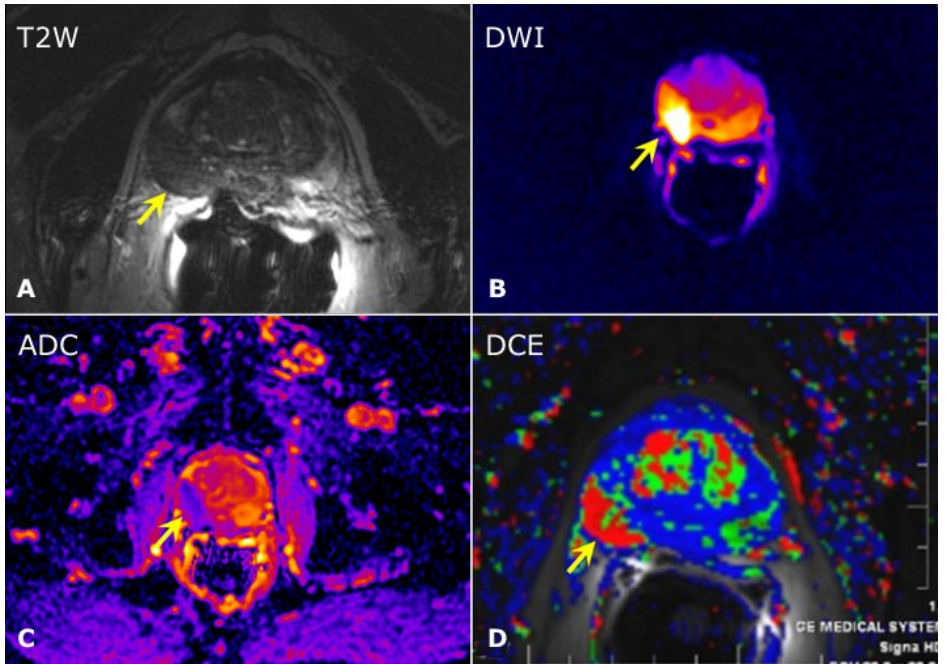
Collaboration with MSKCC

Clinical Motivation

Prostate Cancer

- Prostate cancer (PCa) is the **second leading cause of cancer death** among men in U.S.A.
- Serum biomarker, **prostate-specific antigen (PSA),** is used for screening



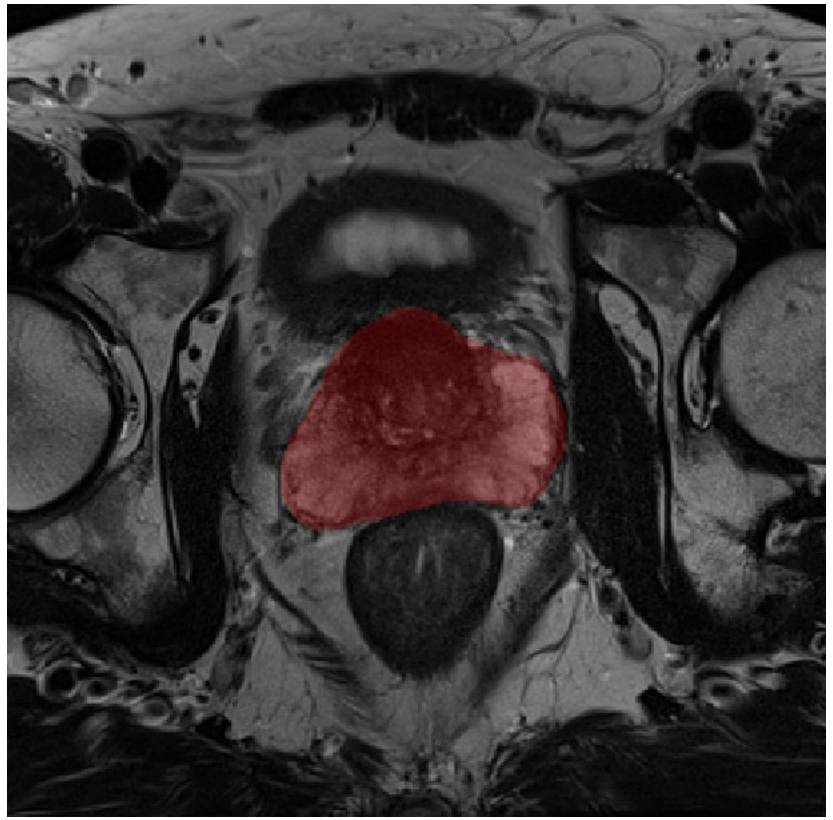


- Need to delineate **aggressive** forms of PCa from **indolent**
  - **Multi-parametric MRI (mpMRI)**

Image Source: Massachusetts General Hospital www.massgeneral.com

Where is the prostate?

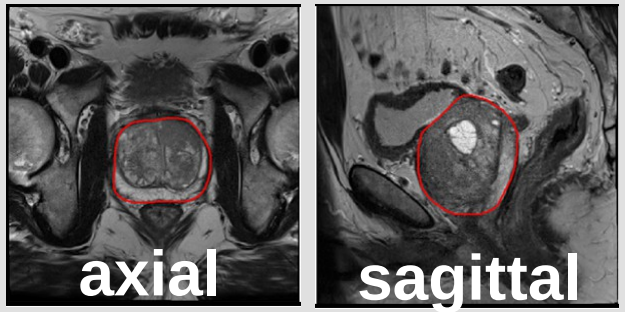
First Things First



Prostate Segmentation
Multi-view MRI

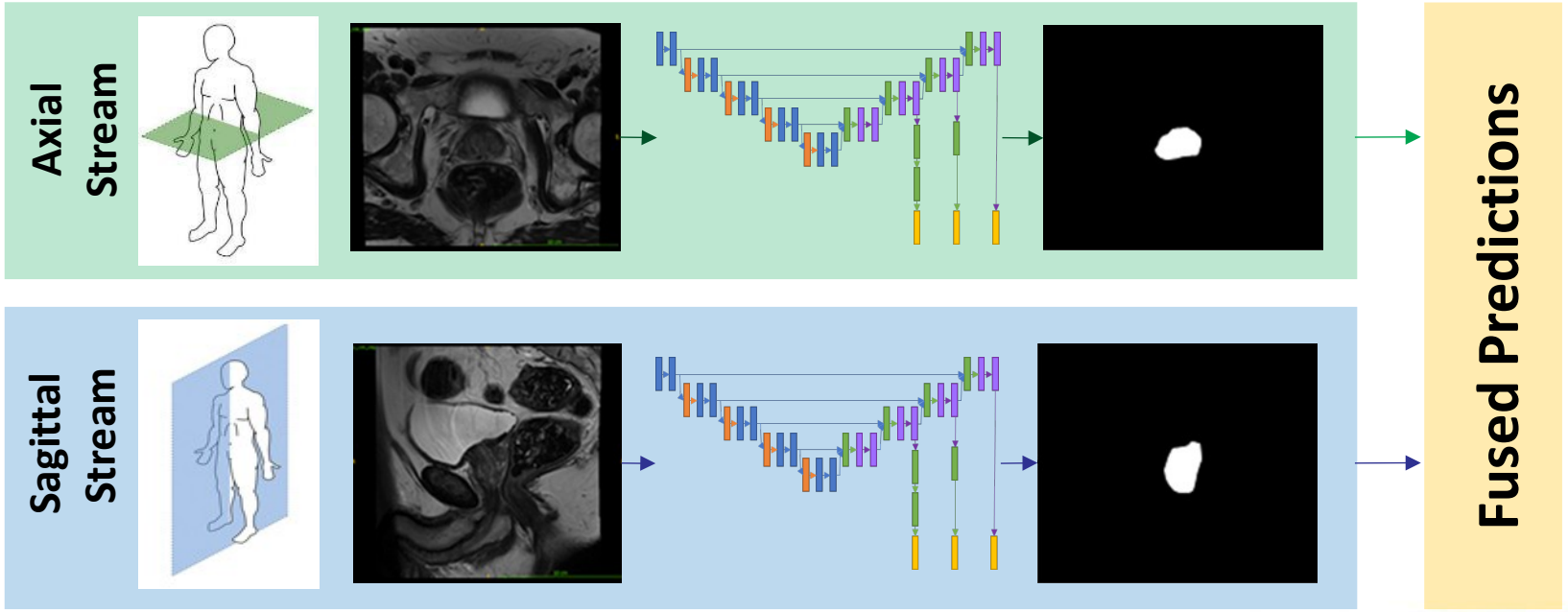
Task

Segment the prostate using ***axial*** and ***sagittal*** MRI views



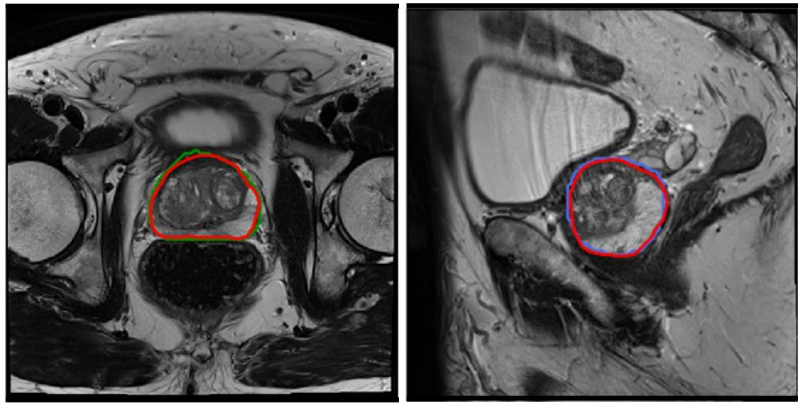
- ProstateX2 (open) DB : **80 patients**
  - 60 train
  - 20 test

- Segmentation : often 1st step in computer-aided systems
  - Need for accurate, automatic, fast and reproducible results
  - Alleviate clinicians from time-consuming tasks



Segmentation Results

DICE Score & Lesions in Segmentations



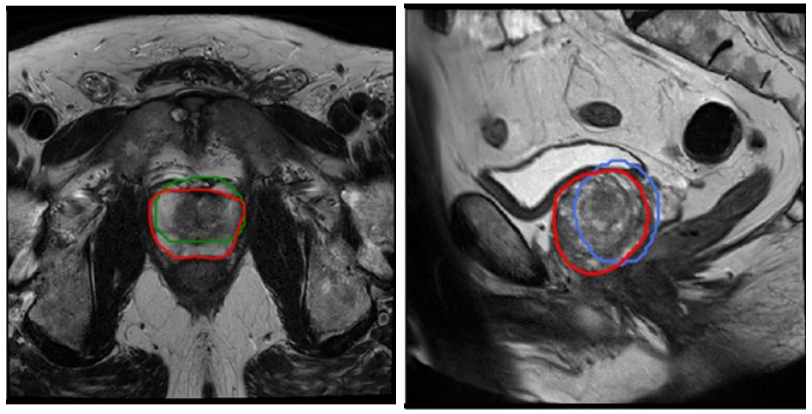
Average DICE Score: **0.81** ± 0.04

Manual Segmentation

Prediction (axial)

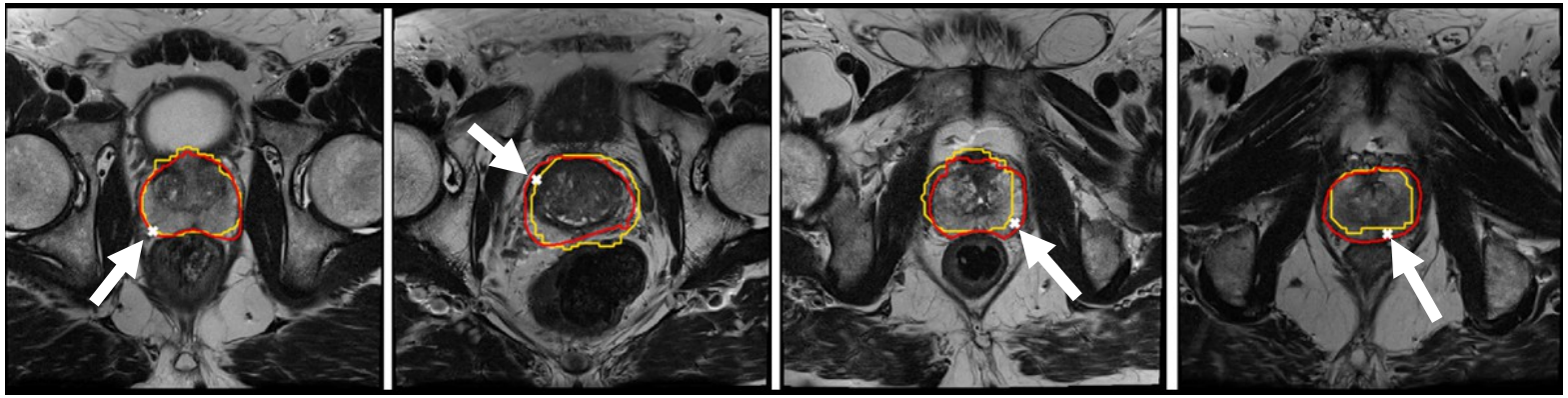
Prediction (sagittal)

Best ⟷ **Worst**



	# Lesions (%)
Multi-planar	18 (82%)
Manual	22 (100%)

Average distance of lesions to contour was 1.60 pixels



Missed lesions in multi-planar segmentations

PSA Recurrence Prediction

Highly ambitious clinical endpoint

Given an mpMRI imaging study of a patient that will undergo a prostatectomy, can we predict if his PSA levels will rise to abnormal levels again?

Memorial Sloan Kettering Cancer Center

- Private DB : **198 patients**
  - 158 train
  - 40 test

Transfer learning: leveraging on non-medical, larger databases

- **ResNet** trained on ImageNet (14M images / 1000 classes)

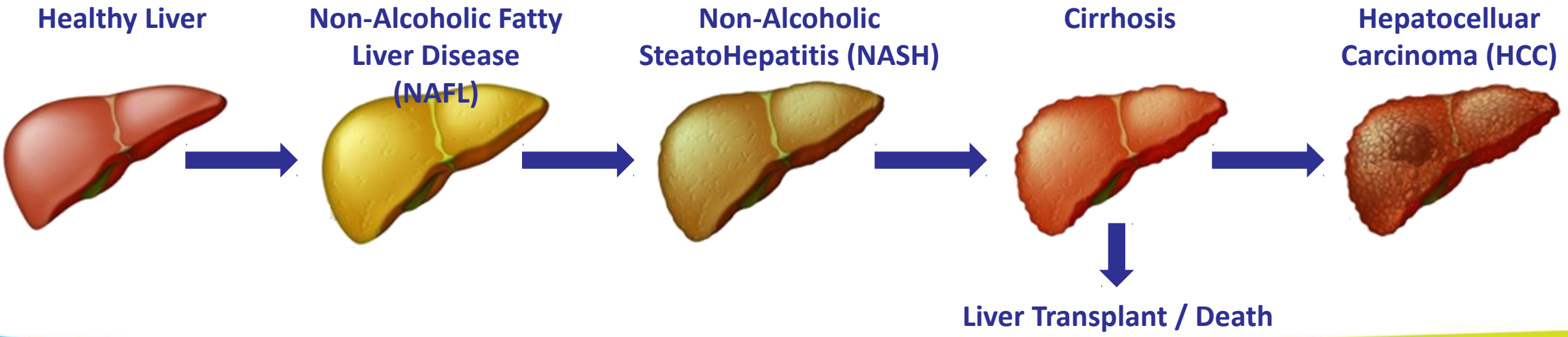
iBiopsy® for *Liver*

Collaboration with UCSD

Clinical Motivation

Non-Alcoholic SteatoHepatitis (NASH)

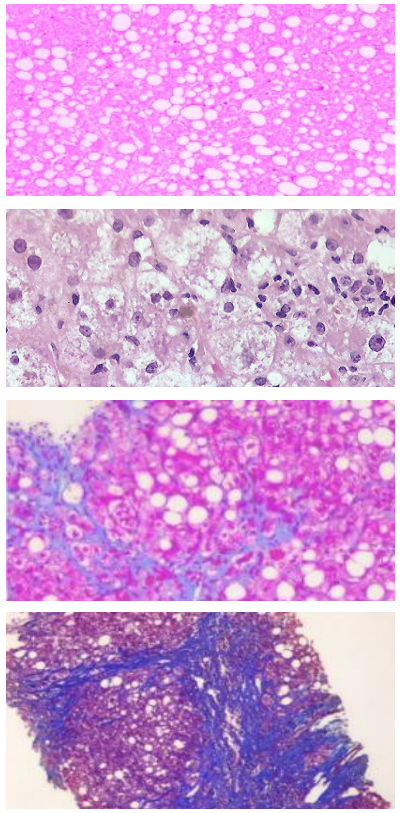
- Liver fat accumulation (steatosis), leading to inflammation, fibrosis and life-threatening cirrhosis
- NASH is now the **second** leading cause of liver transplant in the USA
  - Prevalence between 9-15 million people in the USA, with 15-25% progressing to cirrhosis and liver cancer



Clinical Problem

Diagnosing NASH

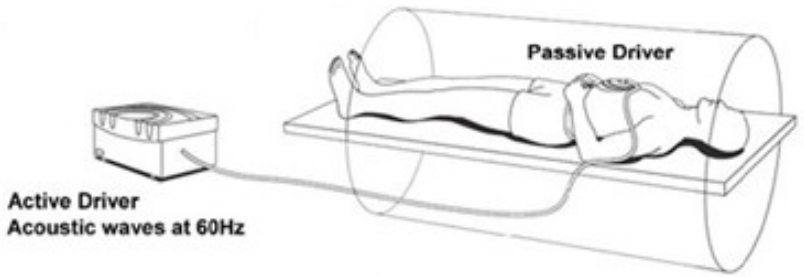
Histological Samples



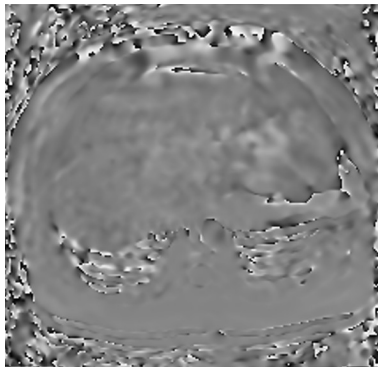
Healthy (CRN 0)

Cirrhosis (CRN 4)

- Current diagnosis is achieved through histological analysis of liver biopsies
  - Fibrosis Stages (CRN) 0 – 4
- **Magnetic Resonance Elastography (MRE)** measures tissue stiffness through the introduction of shear waves and by imaging their propagation using MRI
  - Used as a non-invasive tool to identify liver fibrosis



MRE Phase Image



Liver Stiffness

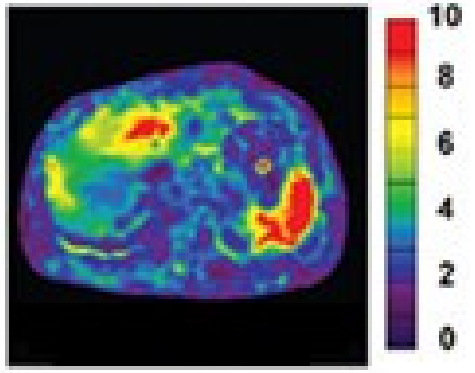


Image Sources: [Ludwig et al, 1980] [Kleiner,et al, 2005] [McPherson et al, 2015] [Singh et al, 2015] https://blog.cincinnatichildrens.org/radiology/mri-elastography/

Fibrosis Staging: Liver Stiffness vs. iBiopsy®

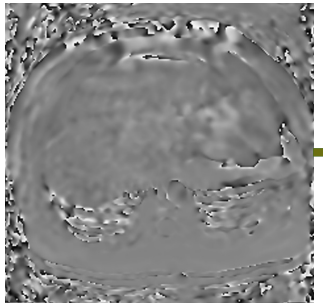
From MRE Phase Image To Fibrosis Classification

Classification Task

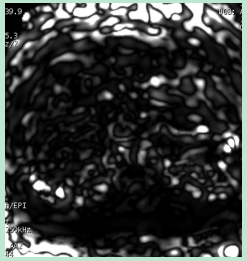
Predict histological fibrosis stage from MRE phase images

- **Two-class** prediction:
  - CRN ≤2
  - CRN ≥3
- DB : **68 patients**
  - 47 train
  - 21 test

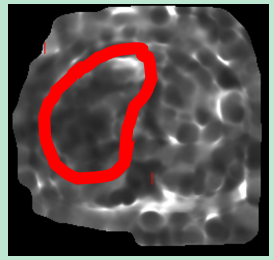
MRE Phase Image



Standard Method (Liver Stiffness)



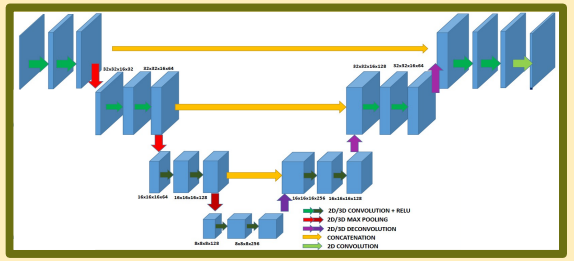
Wave Image + Elastogram



Liver stiffness (kPa)

Average value @ ROI

Median's iBiopsy®



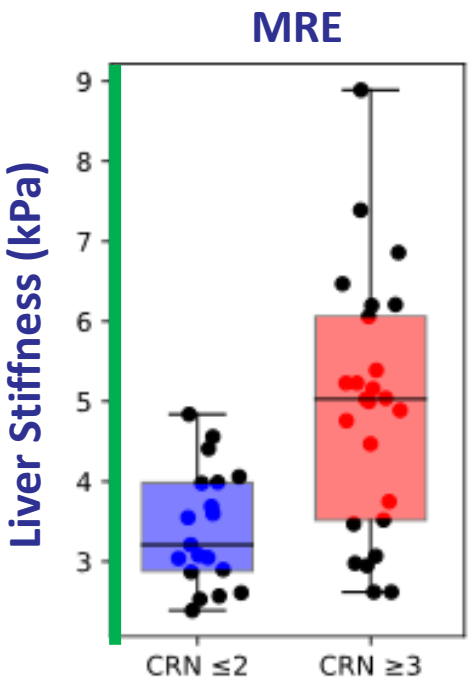
UNET-inspired Network

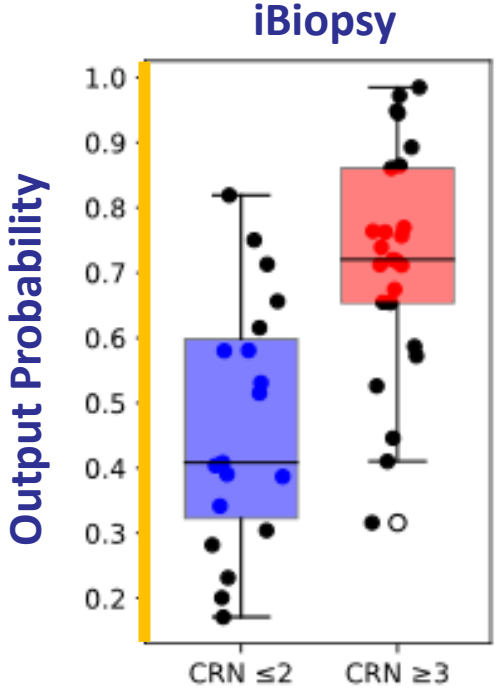
Learned Fibrosis Map

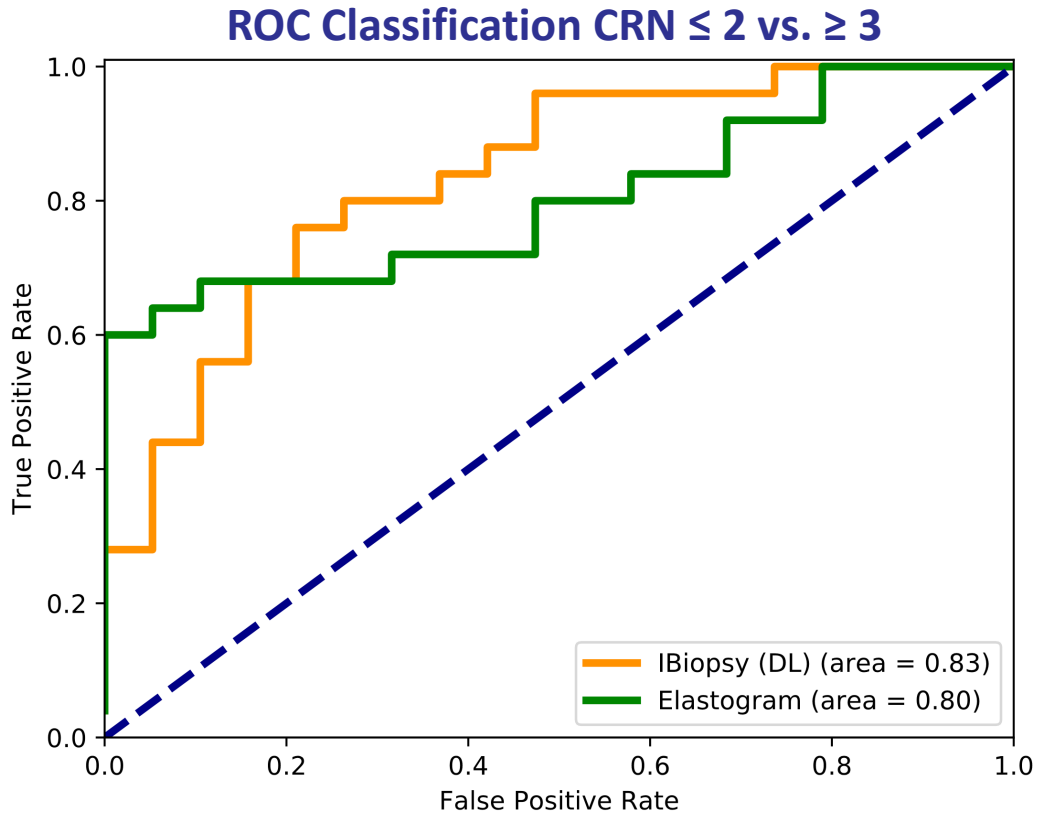
Average value @ ROI

Fibrosis Staging: Liver Stiffness vs. iBiopsy®

Results on Test Dataset







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Encryption For Medical Imaging

Collaboration with Microsoft Research

Private Analysis of Medical Data

Homomorphic Encryption

- Privacy concerns about personal data are on the rise, particularly sensitive information like medical data

HAVE data
NEED analytics

HAVE tools for analysis
NEED data

- Traditional encryption schemes prevent computation on data without decrypting it first

- **Homomorphic encryption** [1] allows computations while keeping the customer's data protected
  - Simple linear operations (+ and ×) are possible; others can be approximated using Taylor expansion
  - **Data analysis is done on encrypted data**

[1] Craig Gentry. Fully homomorphic encryption using ideal lattices. In STOC, volume 9, pages 169–178, 2009.

Homomorphic Encryption

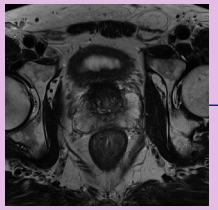
Proof of Concept : Prostate Cancer Tumor Analysis

LOCAL CLINICAL CENTER

Clinical Question
Benign or malignant tumor? (0/1)

Feature Extraction
e.g. Haralick Features

Encoding Stage
polynomial representation modulus **n=8192**, base **2**



$$\begin{bmatrix} 13{,}625 \\ 0{,}75 \\ 1{,}125 \\ 5{,}25 \end{bmatrix} \rightarrow \begin{bmatrix} P(X) = X^3 + X^2 + 1 - X^{n-1} - X^{n-3} \\ P(X) = -X^{n-1} - X^{n-2} \\ P(X) = 1 - X^{n-3} \\ P(X) = X^2 + 1 - X^{n-2} \end{bmatrix}$$

THIRD PARTY – DATA ANALYSIS

Encryption Stage
polynomials modified with key Q

$$\begin{bmatrix} P(X) = -X \\ P(X) = X^2 + X + 1 \\ P(X) = X^4 + 1 \\ P(X) = X^3 + X^2 \end{bmatrix}$$

ENCRYPTED Analysis
e.g. logistic regression (with Taylor approximation)

$$[P(X) = X^4 + X^3 + 2X^2 + 2]$$

Decryption Stage
Decryption with key D

$$[P(X) = -X^{n-1} - X^{n-2} - X^{n-3}]$$

Decoding Stage
final diagnosis only known to clinical center

Malignant Tumor $[0{,}875]$

Closing Remarks

Closing Remarks

- Deep learning has great potential in computer aided diagnosis
  - Prostate, lung and liver examples to name a few
- Homomorphic encryption for private data analysis

We are hiring!

www.mediantechnologies.com

Research Scientist - (SC0118C)

Requisition #	SC0118C
Job Title	Research Scientist
Contract Type	Permanent
Weekly working hours	Full time
Job Classification	
Career Level	Junior (2-4 years)
Education (minimum)	PhD
Travel	
Category	Science and Image Processing

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The Imaging Phenomics Company®

Our Core Values

Leading innovation with purpose
Combine the spirit of innovation with our passion and conviction to help cure cancer and other debilitating diseases.

Committing to quality in all we do
Be dedicated to quality in everything we do. Quality begins with us and we are committed to it.

Supporting our customers in achieving their goals
Listen to the needs of our customers and help make their goals our goals through our innovation, imaging expertise, superior services and quality solutions.

Putting the patient first
There is a person at the other end of the images we analyze who is counting on us to do everything we can to help make them healthier.

Lauréat du PASS FRENCH TECH

ELIGIBLE PEA PME

ALMDT EURONEXT GROWTH