A Machine-Learning Approach to Differentiating Benign and Malignant Peripheral Nerve Sheath Tumors

A Multicenter Study

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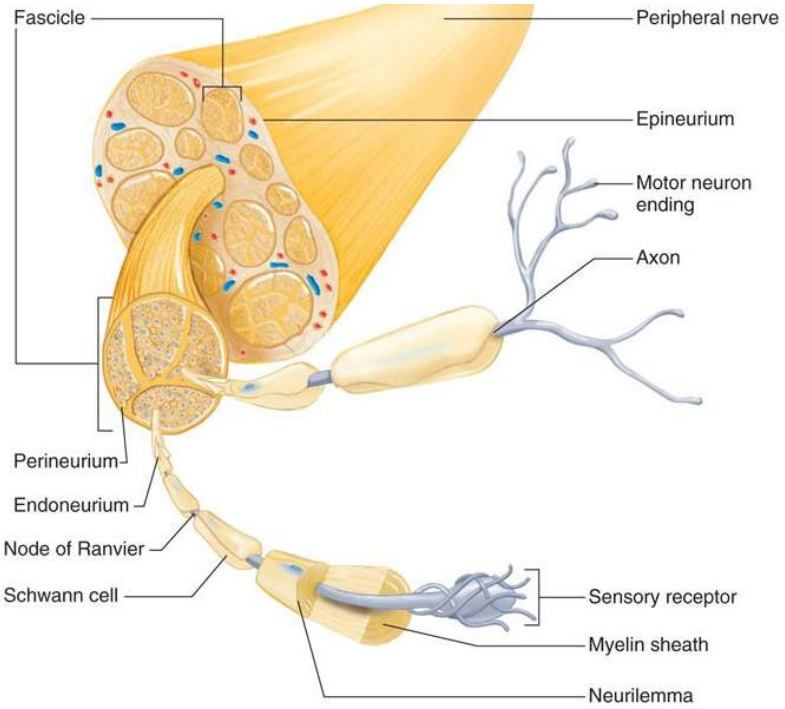
10.21.20

Outline

- **Background:**
  - **Benign and Malignant PNST**
  - **Current Clinical Workflow**
- Methods:
- Results
- Future Directions

Goal: Develop a binary classifier using MRI information, providing early diagnosis of Benign and Malignant peripheral nerve sheath tumors (**PNSTs**)

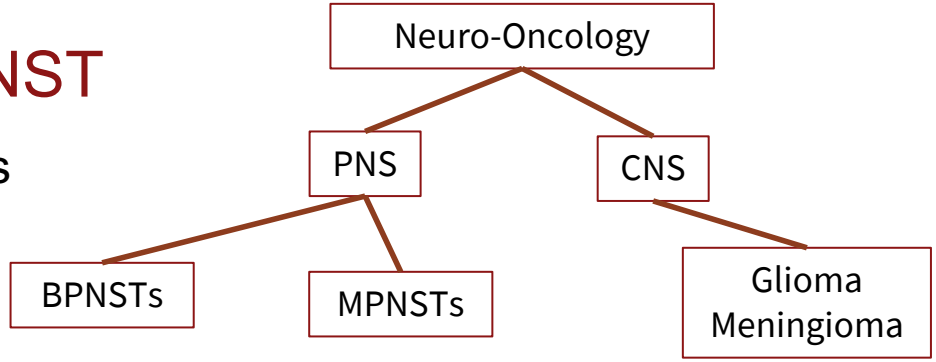


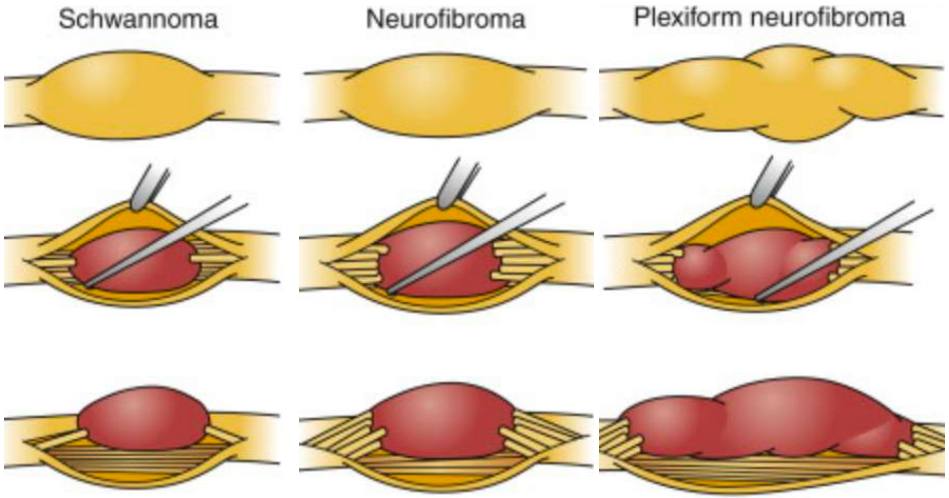
Benign and Malignant PNST

Peripheral Nerve Sheath Tumors

(outside the brain and spine)

- Benign (BPNSTs)
  - Schwannoma
  - Neurofibroma
  - Perineuroma
  - Hybrids
  - Ganglioneuroma
- Malignant (MPNSTs)

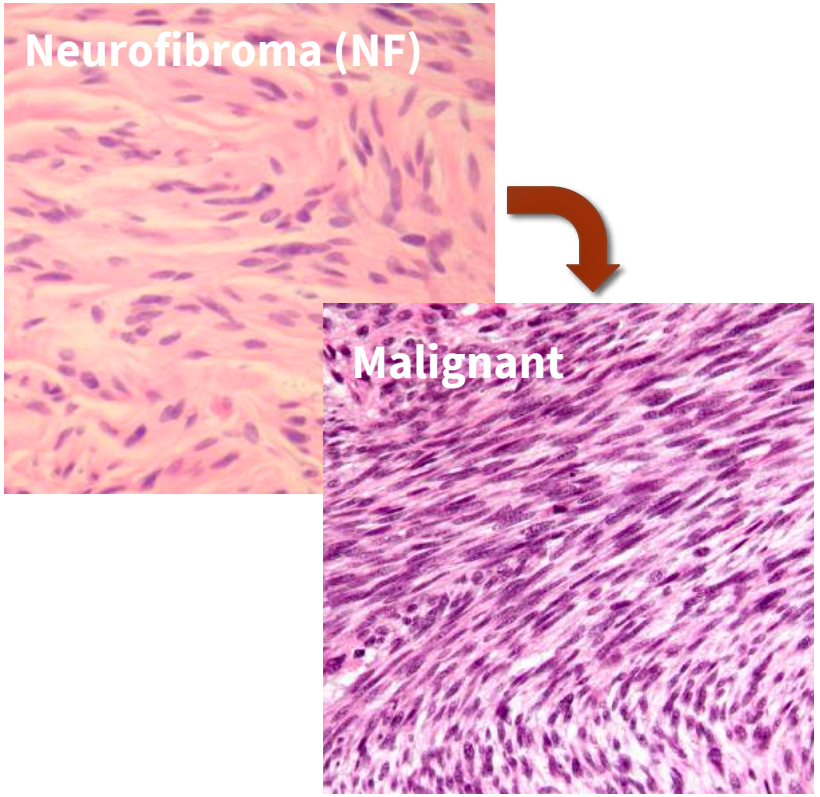




MPNSTs – Can't Miss Diagnosis

- Natural History
  - **5-year survival 30-50%**
  - 50% of all MPNSTs occur in Neurofibromatosis (NF1)
  - 5-10% of NF1 patients will develop MPNSTs

- Pathophysiology
  - **Malignant Transformation**
  - Neurofibroma → Malignancy
  - Invasion and metastasis → morbidity & **surgical difficulty**

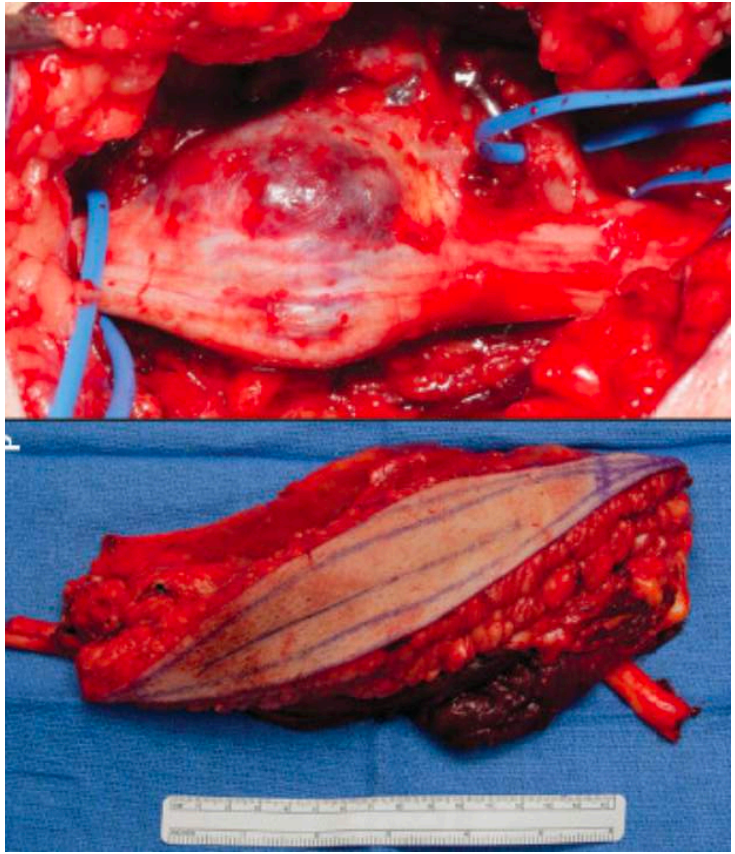


Surgical Morbidity – Complex

MPNST, Surgical Goal: complete resection – **total resection is curative** – with minimal disruption of nerve function

Surgical Challenges

- Greater nerve fiber invasion
- Neighboring tissue invasion
- Needs wide excisional margins
- Must avoid seeding
- Expect repeat surgery



Surgical Morbidity – Simple

BPNSTs are surgically simpler

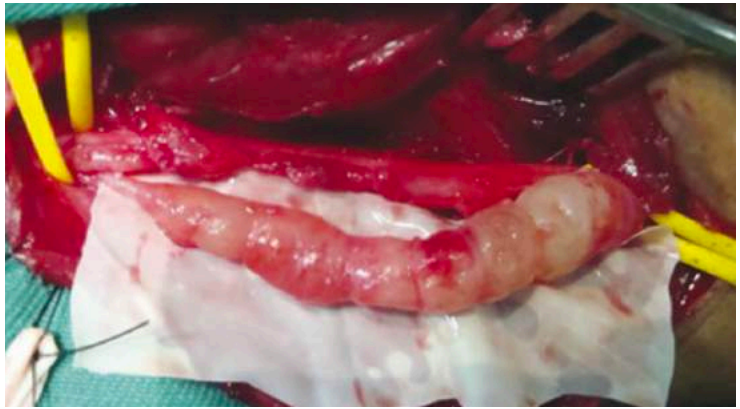
- Local involvement
- Low recurrence potential

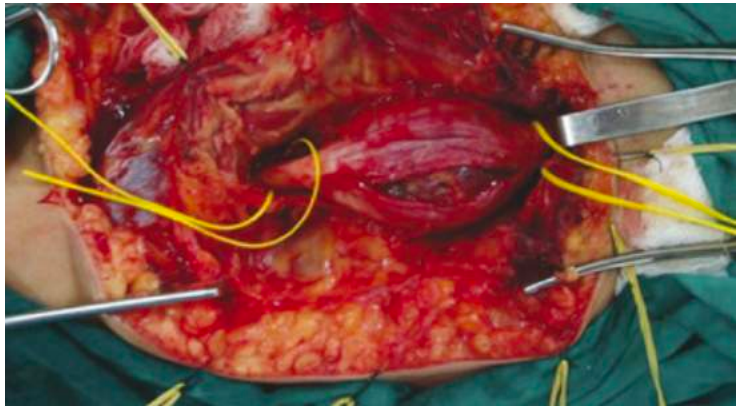
Schwannoma:

- Tumor of supporting Schwann cells
- Single nerve fiber
- Tumor displaces uninvolved fascicles

Neurofibroma:

- Tumor of the endoneurium
- Single or multiple nerves
- Possible functional implications





A Need for Early Diagnosis by Imaging

Accurate imaging can aid surgical planning to maximize quality of life

- Resect MPNSTs earlier
- Avoid unnecessary surgery

Imaging Options

- **MRI:** qualitative and semantics
- **PET:** SUV > 3.5
- **Gold Standard: Surgical Biopsy**

Wasa et al. - MRI Criteria

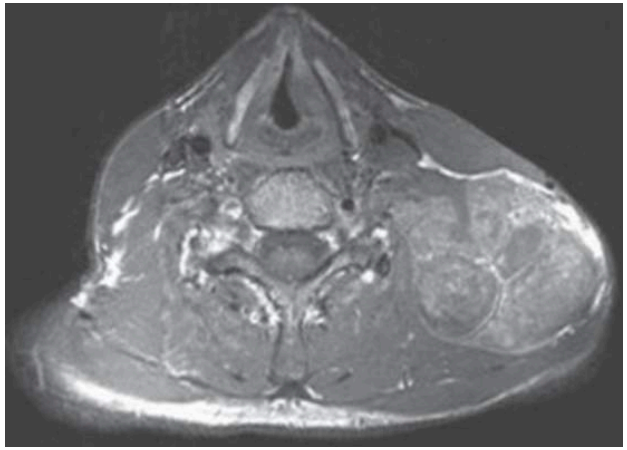
With 2 of 4 – 61% sens, 90% spec

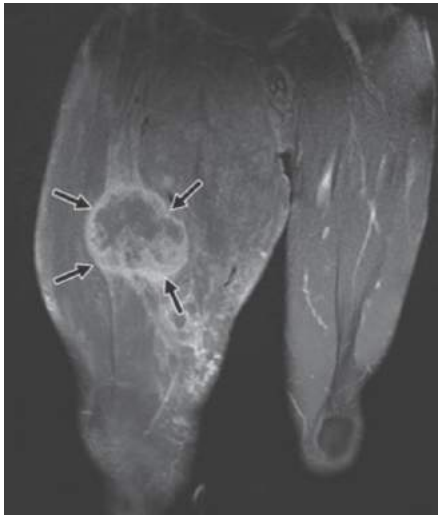
1. Diameter > 5 cm
2. Peripheral tumor enhancement
3. Perilesional edema
4. Intra-tumoral cyst

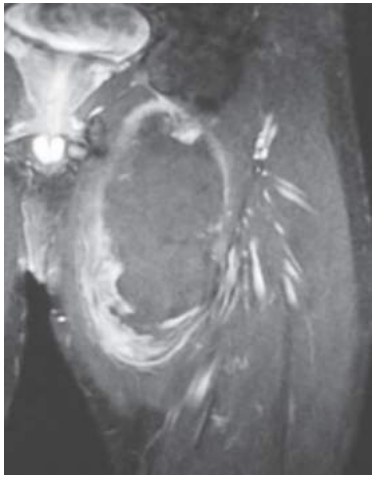
Radiographic Ambiguity

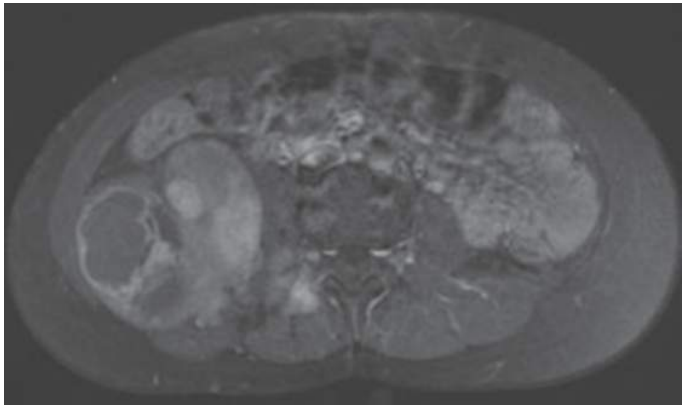
MRI T1 with Gad Fat Sat commonly available

- Neck – NF1
- Right Thigh – MPNST
- Left Thigh – MPNST
- Right RP – MPNST









Additional Tools: PET, Derlin et al.

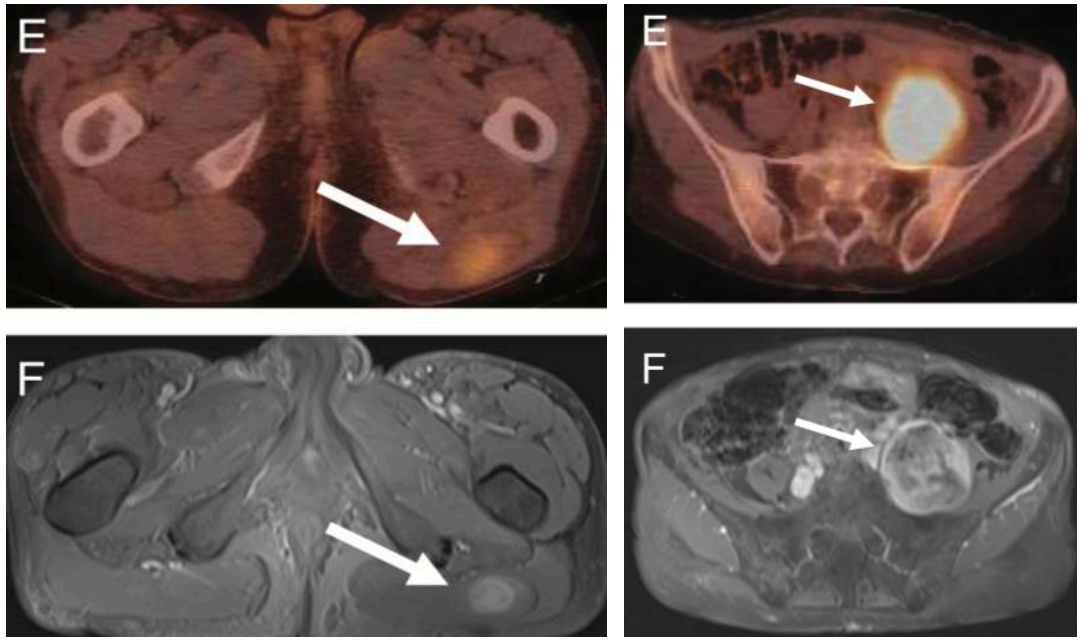
PET – less available

SUVmax ≥ 3.5

- 100% Sensitive
- 54.5% Specific
- 47.4% PPV

MRI comparison

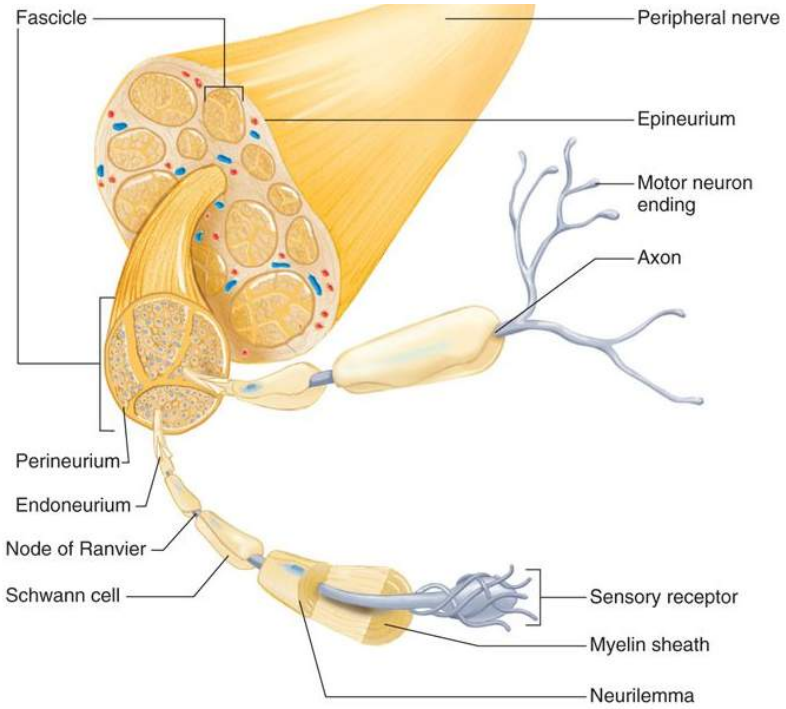
- 66.7% sensitive
- 90% specific
- 75% PPV



Outline

Goal: Develop a binary classifier (MPNST vs BPNST) with MRI

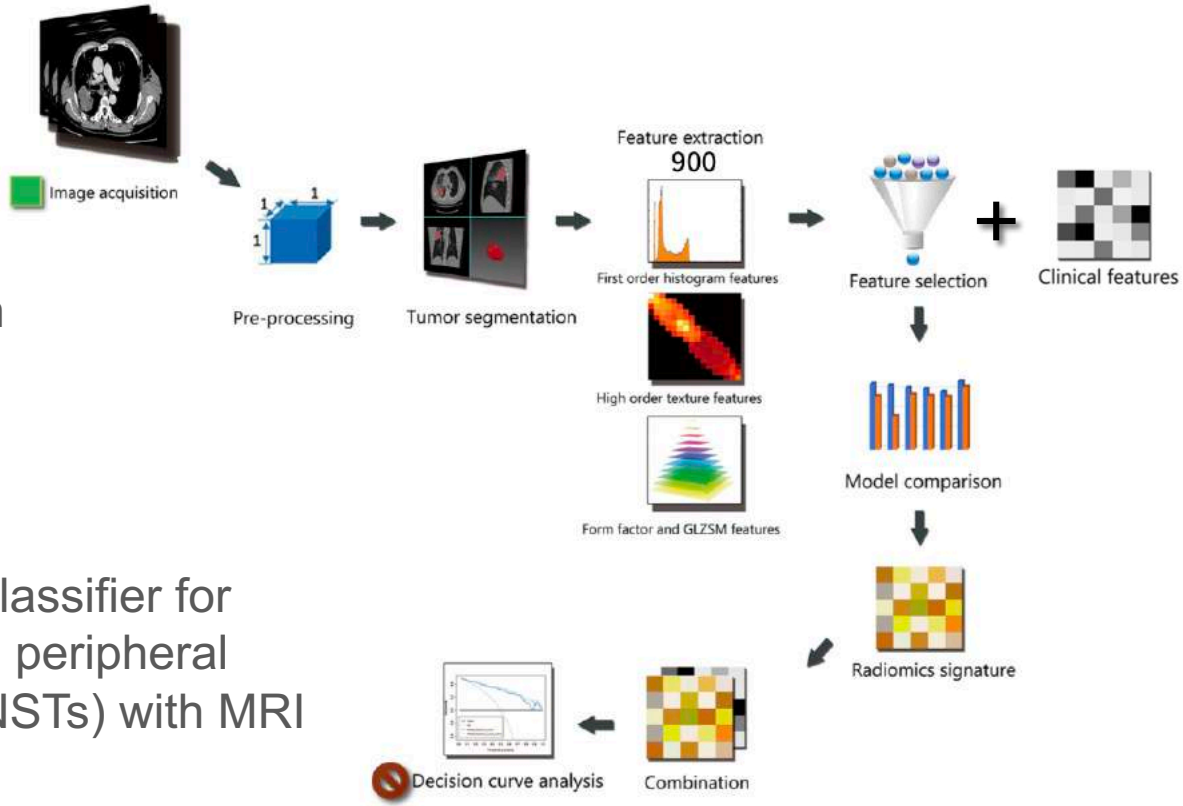
- Background:
- **Methods:**
  - **Segmentation**
  - **Clinical data collection**
  - **Feature**
    - **Extraction**
    - **Selection**
    - **Optimization**
  - **Prediction Analysis**
- Results
- Future Directions



Workflow

- **Input**: MRI T1-gad with Fat Suppression
  - › Most available

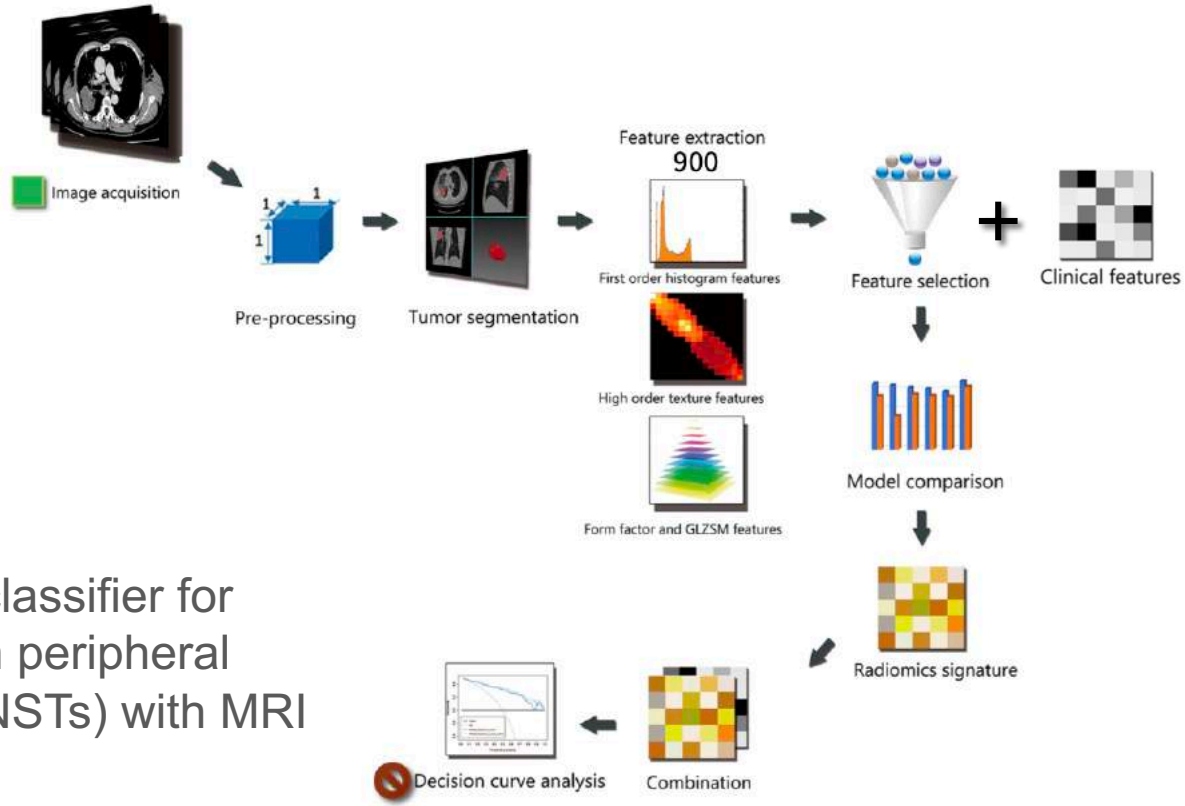
- **Output**: Classification probability and label
  - › MPNST or BPNST



Goal: develop a binary classifier for Malignant versus Benign peripheral nerve sheath tumors (PNSTs) with MRI

Radiomics Workflow

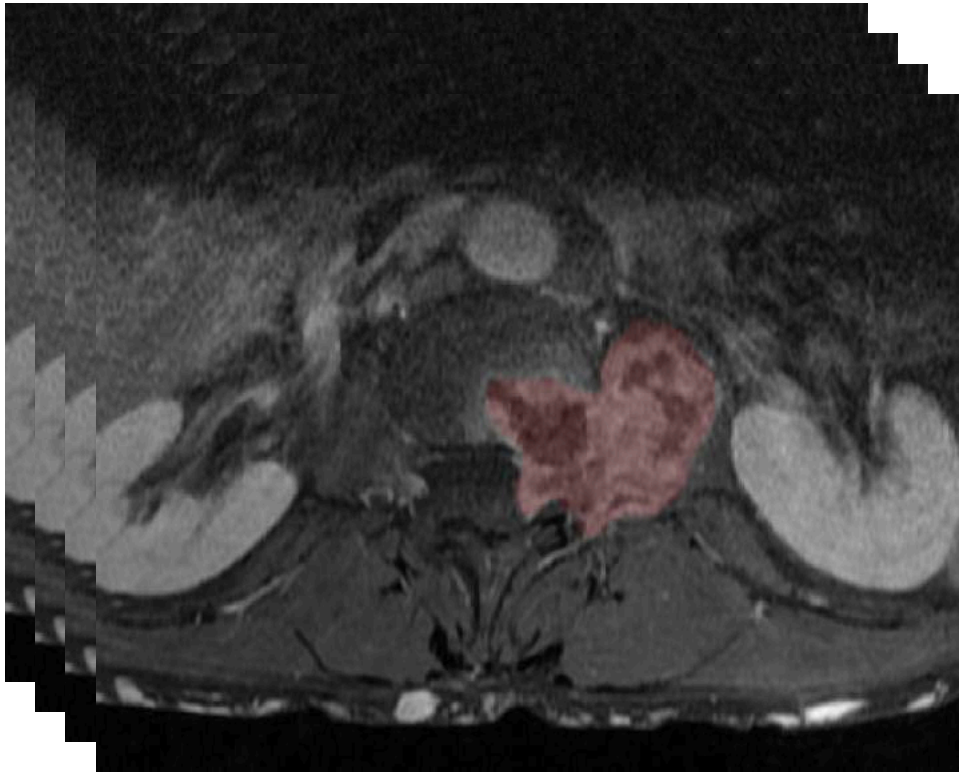
- Image segmentation
- Clinical data collection
- Feature
  - Extraction
  - Selection
  - Optimization
- Prediction Analysis



Goal: develop a binary classifier for Malignant versus Benign peripheral nerve sheath tumors (PNSTs) with MRI

Images and Segmentation

- **Imaging Segmentation**
  - **171 Benign**
  - **95 Malignant**
  - **SHC, Uni. Utah, Mayo**
- Clinical data collection
- Feature
  - Extraction
  - Selection
  - Optimization
- Prediction Analysis

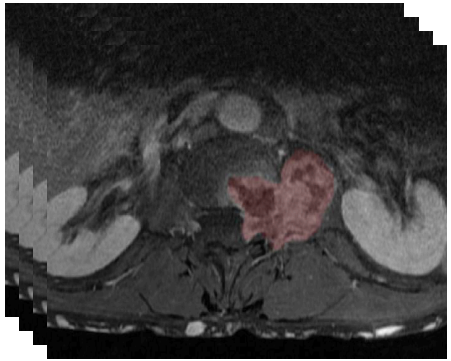


Clinical Features

- Chart review
- Red Flag symptoms of MPNSTs/infiltrative tumors
  - Pain
  - Rapid growth
  - Neurological deficits

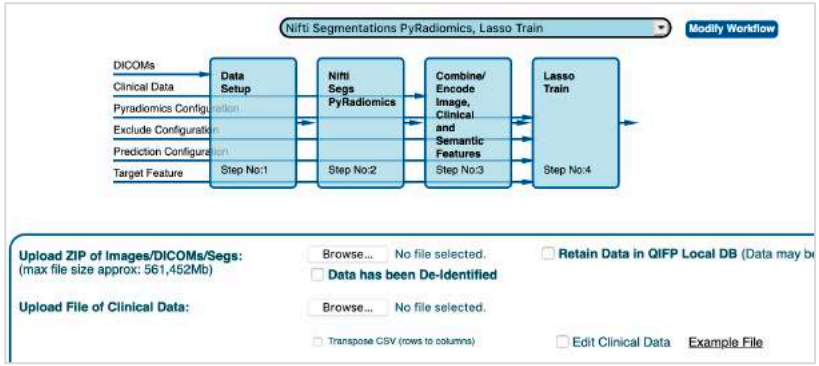
	Benign (N = 171)	Malignant (N = 95)	p-Value
Age, yrs. (SD)	45.5 (15.3)	43.3 (18.2)	0.320
Sex			0.042
Male	75 (44%)	54 (57%)	
Female	96 (56%)	41 (43%)	
Spontaneous Pain	41 (24%)	71 (75%)	<0.001
Motor Deficit	45 (26%)	31 (33%)	0.275
NF1	38 (22%)	41 (43%)	<0.001
NF2	10 (6%)	0 (0%)	0.016
Schwannomatosis	5 (3%)	0 (0%)	0.164

Feature Extraction



- Quantitative Imaging Feature Pipeline (Stanford, Napel)
- Upload NifTI segmentations
- Pyradiomics Package: 900 standardized features

QIFP: Home Page



Feature Selection – Preliminary Model

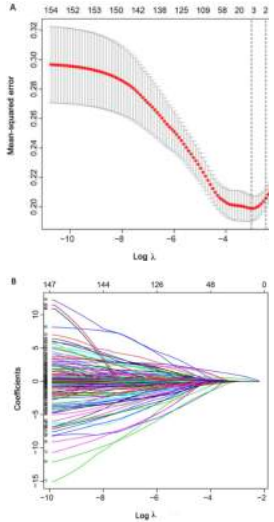
1. LASSO
   - 70:30 Train Test Split
   - R, glmnet-package
   - 10x Cross Validation
   - 1000 cycles

2. Preliminary model
   - 80% selection
   - **21 Features (from 900)**
     - **19 Textural**
     - **2 Clinical**

1. 900 Initial Features

- `First Order Statistics` (19 features)
- `Shape-based (3D)` (16 features)
- `Shape-based (2D)` (10 features)
- `Gray Level Cooccurence Matrix` (24 features)
- `Gray Level Run Length Matrix` (16 features)
- `Gray Level Size Zone Matrix` (16 features)
- `Neighbouring Gray Tone Difference Matrix` (5 features)
- `Gray Level Dependence Matrix` (14 features)

2. Error Reduction



3. 21 Selected Features

1	Intercept	2.21727218721519
2	log-sigma-5-mm-3D_glrlm_RunLengthNonUniformity	0.387899557771315
3	wavelet-HHL_glcm_MaximumProbability	0.175997193985862
4	wavelet-LHL_glrlm_RunVariance	0.175501773912802
5	original_shape_Maximum2DDiameterRow	0.170282978191518
6	original_glrlm_LongRunEmphasis	0.168658168332157
7	original_shape_Maximum2DDiameterColumn	0.156694553330967
8	log-sigma-5-mm-3D_glszm_GrayLevelNonUniformity	0.131656590446044
9	[illegible]Energy	0.123258921624558
10	log-sigma-5-mm-3D_firstorder_Skewness	0.107173356877628
11	log-sigma-5-mm-3D_firstorder_Maximum	0.089609832309113 9
12	wavelet-HLL_glszm_LargeAreaHighGrayLevelEmphasis	0.035471622286746
13	log-sigma-3-mm-3D_firstorder_Energy	0.004102186499879 62
14	wavelet-LHL_firstorder_Energy	0.003516602191487 43
15	log-sigma-3-mm-3D_firstorder_TotalEnergy	0.003510839394397 8
16	original_firstorder_TotalEnergy	6.328939691183 43e-15
17	wavelet-LHL_firstorder_TotalEnergy	3.090991687797 73e-16

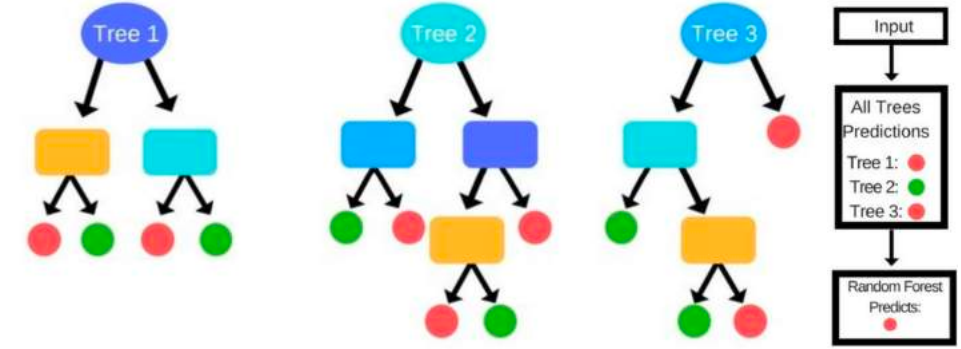
Feature Selection – Optimized Model

- Imaging Segmentation
- Clinical data collection

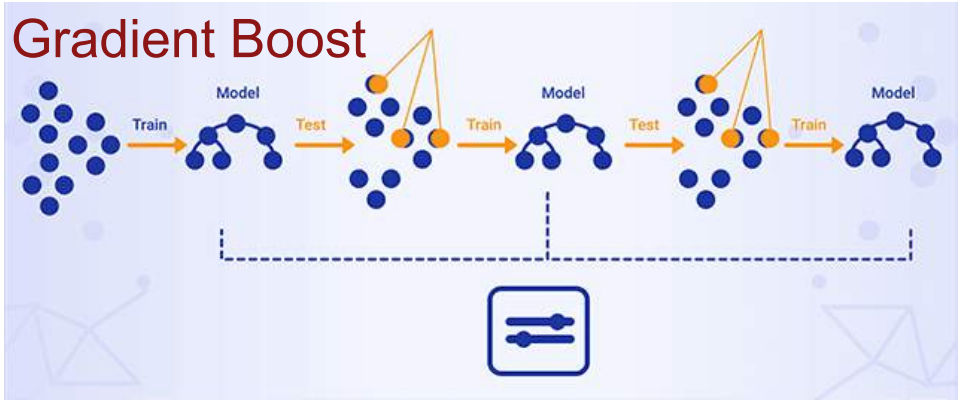
- Feature
  - › Extraction
  - › Selection
  - › **Optimization**
    - **caret package**
    - **21 features, ranked**

- Prediction Analysis

Random Forest



Gradient Boost



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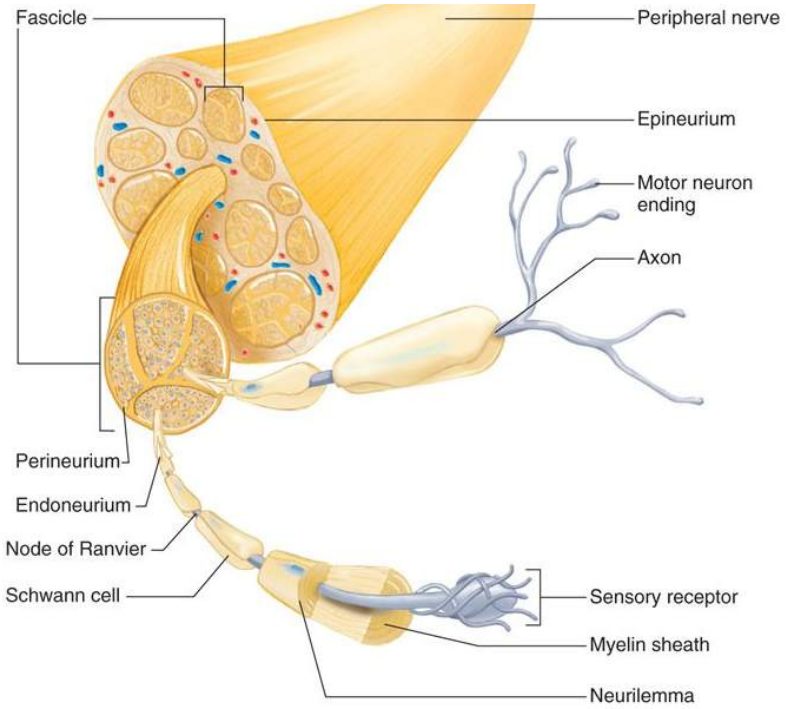
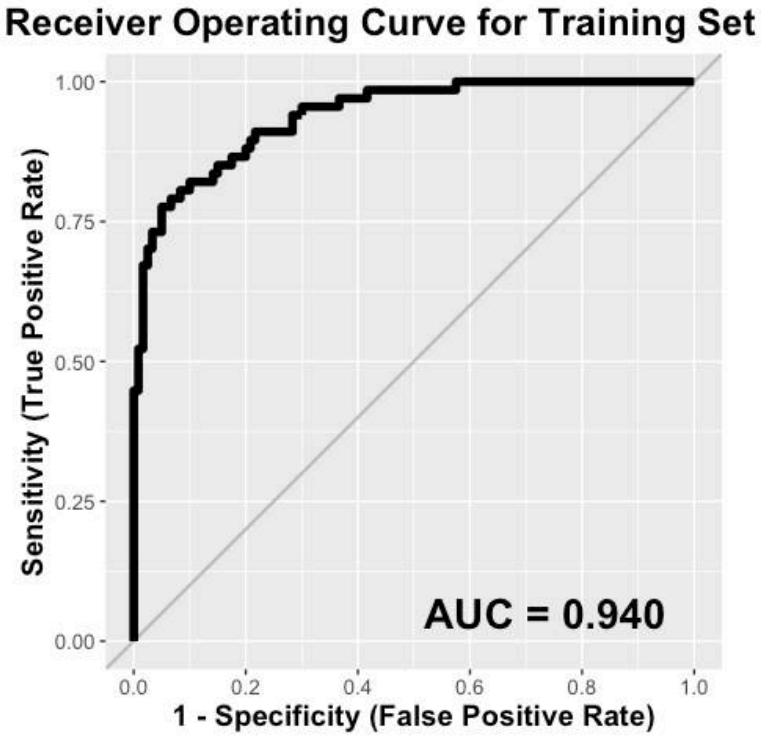
Goal: Develop a binary classifier (Malignant/Benign) with MRI

- Background:
- Methods:
- **Results**
  - **1. Texture + Clinical**
  - **2. Texture Only**
  - **3. Clinical Only**
  - **4. Comparison to Human**
- **Future Directions**



1. Clinical + Texture: AUCs

A



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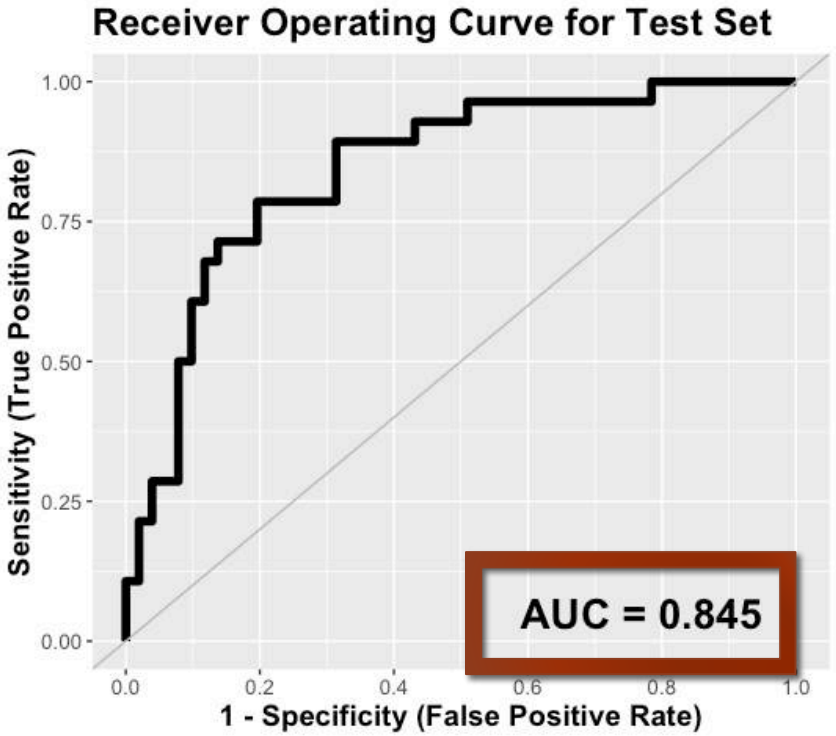


2. Comparison to Human Readers

- Two of each training level
- Two trials
  - 1. Imaging + Clinical
  - 2. Imaging only
- Imaging:
  - T1W, post-gad, fat-sat +
  - T2W or proton-density images, when available

	Sensitivity	Specificity	PPV	NPV
Medical Student	0.518	0.775	0.538	0.752
PN Surgery Fellow	0.625	0.814	0.648	0.798
PN Surgeon	0.821	0.667	0.575	0.872
Radiologist	0.839	0.676	0.588	0.896
Overall	0.684	0.742	0.589	0.823
			AUC	0.704

	Sensitivity	Specificity	PPV	NPV
Medical Student	0.661	0.725	0.569	0.796
PN Surgery Fellow	0.554	0.775	0.577	0.759
PN Surgeon	0.821	0.686	0.590	0.875
Radiologist	0.839	0.686	0.597	0.898
Overall	0.704	0.723	0.582	0.826
			AUC	0.702

Conclusions and Limitations

- Radiomics Classifier Outperforms Human readers

- Radiomics
  - Sensitivity 0.676
  - Specificity 0.882

- Humans
  - Sensitivity 0.839
  - Specificity 0.686

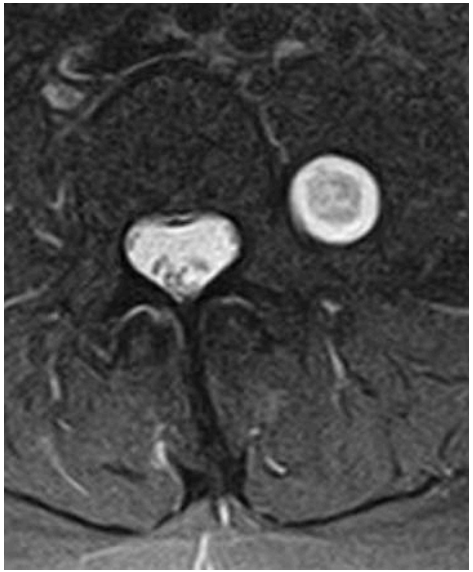
- Imaging Availability
  - Axial view only
  - T1W only
  - Acquisition technique: fat saturation, contrast quality

- Patient heterogeneity: brachial plexus, arm, wrist

- Segmentation vs Semantics

Semantics not captured by segmentations

BPNST:
Neurofibroma
-Target sign



BPNST:
Schwannoma
-Split fat sign

MPNST
-Absent split
fat sign

MPNST
-Perilesional
edema

Acknowledgements

Radiology
- Dr. Kristen Yeom
- Dr. Sam Gambhir
- Dr. Heike Daldrup-Link

PNST Team
- Dr. Elizabeth Tong
- Dr. Thomas Wilson
- Dr. Mark Mahan
- Lydia Tam
- Edward Lee

QIFP Team
- Professor Sandy Napel
- Sarah Mattonen
- Dev Gude

Stanford Neurosurgery
- Dr. Gary K. Steinberg
- Dr. Gerald Grant
- Dr. Gordon Li