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The Effect of Dose on the Onset and Progression of Radiation Induced Brain Necrosis in the Rodent Model

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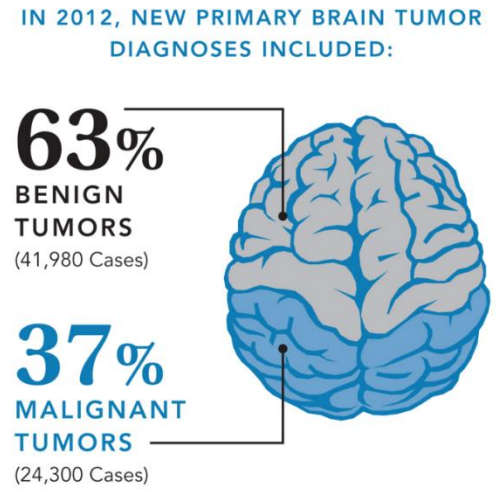
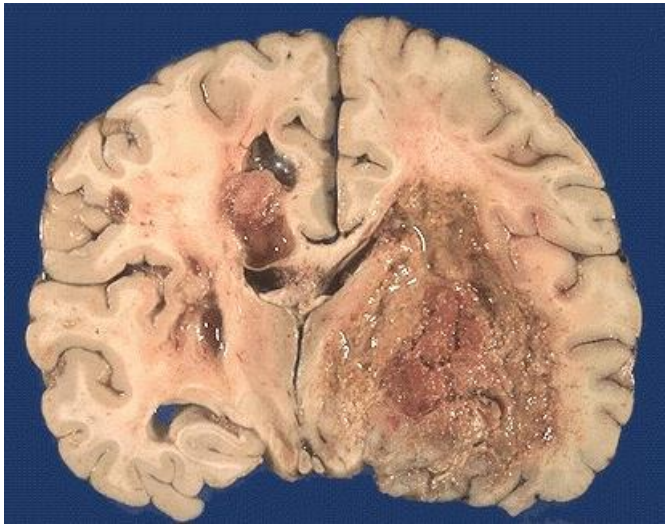
Background: Radiation Induced Necrosis

- Brain Tumor
  - 700,000 people in the US are living with primary brain tumor
  - 3.7 billion dollars is spent on treatment
- Standard Care Treatments
  - Surgical Resection
  - Chemotherapy
  - Radiotherapy
- Radiation Induced Brain Necrosis
  - Develops after radiotherapy
  - Occurs when a high dose of radiotherapy is administered
  - Risks are higher in stereotactic radiosurgery



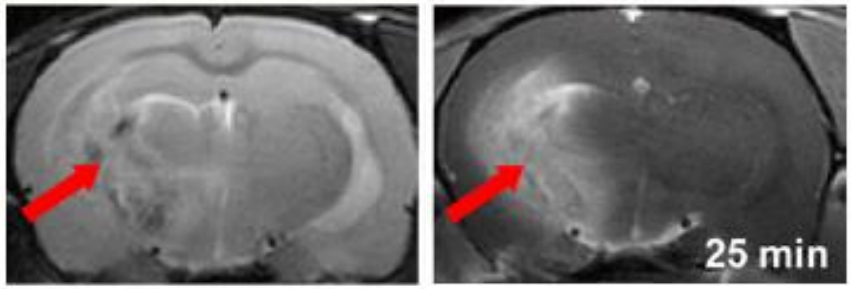
http://braintumor.org/brain-tumor-information/



http://library.med.utah.edu/WebPath/CNSHTML/CNS136.html

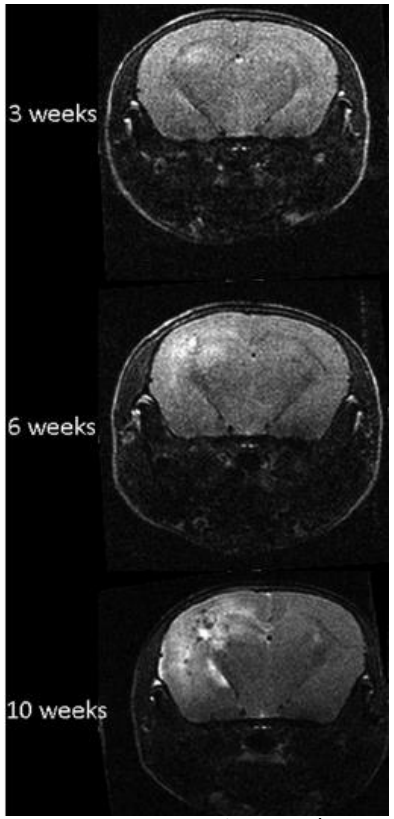
Motivation

- Clinical Problems
  - Lack of clearly defined region
  - No single imaging modality has been sufficiently specific to establish a diagnosis



Wang et al. 2011

- Brain Necrosis Studies
  - No indication of why a certain dose is chosen
  - Different dose results in same pathology, but limited data on rodent



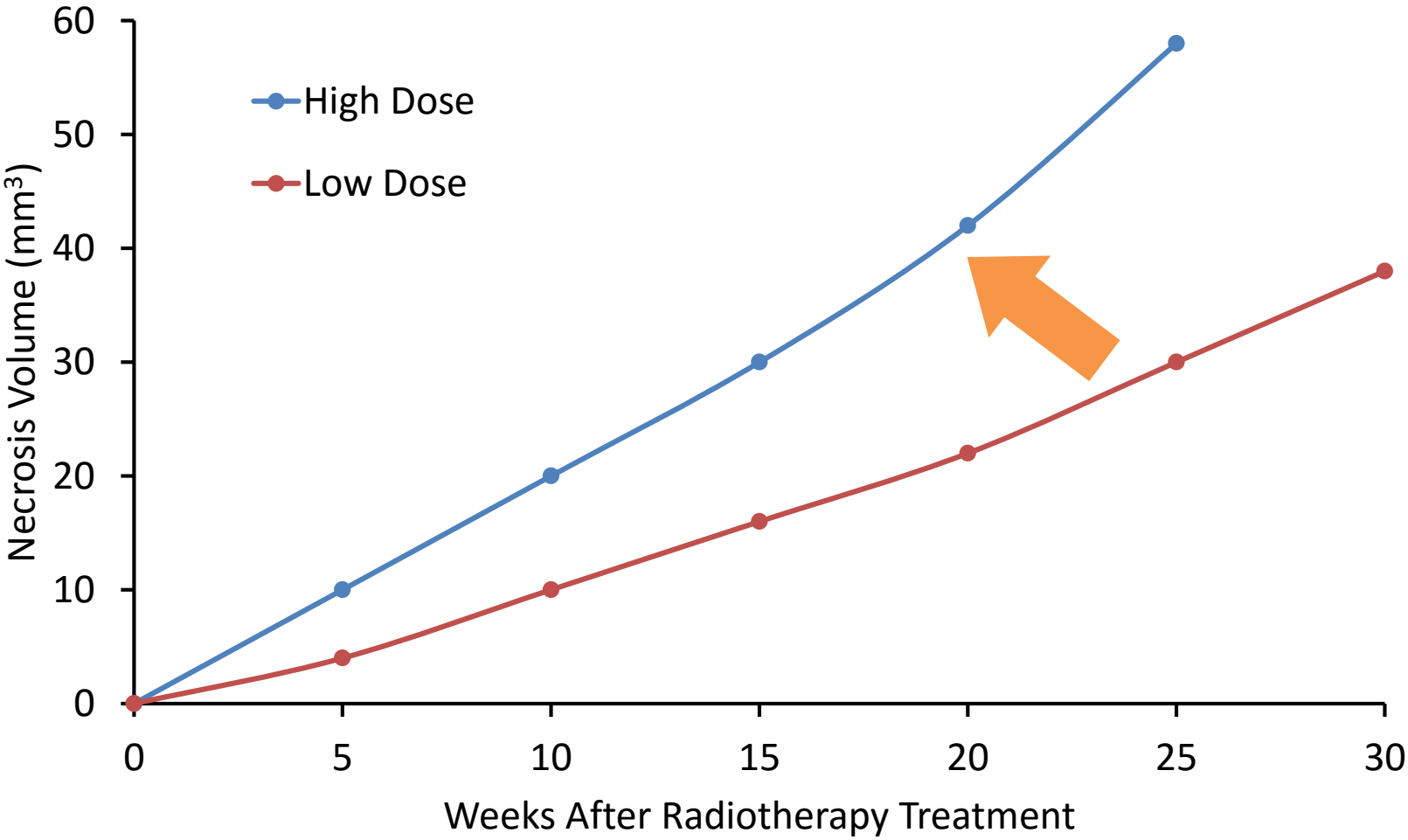
Jiang et al. 2014

Hypothesis

Changing the radiotherapy dose will change the volume progression and the time to onset of radiation induced brain necrosis

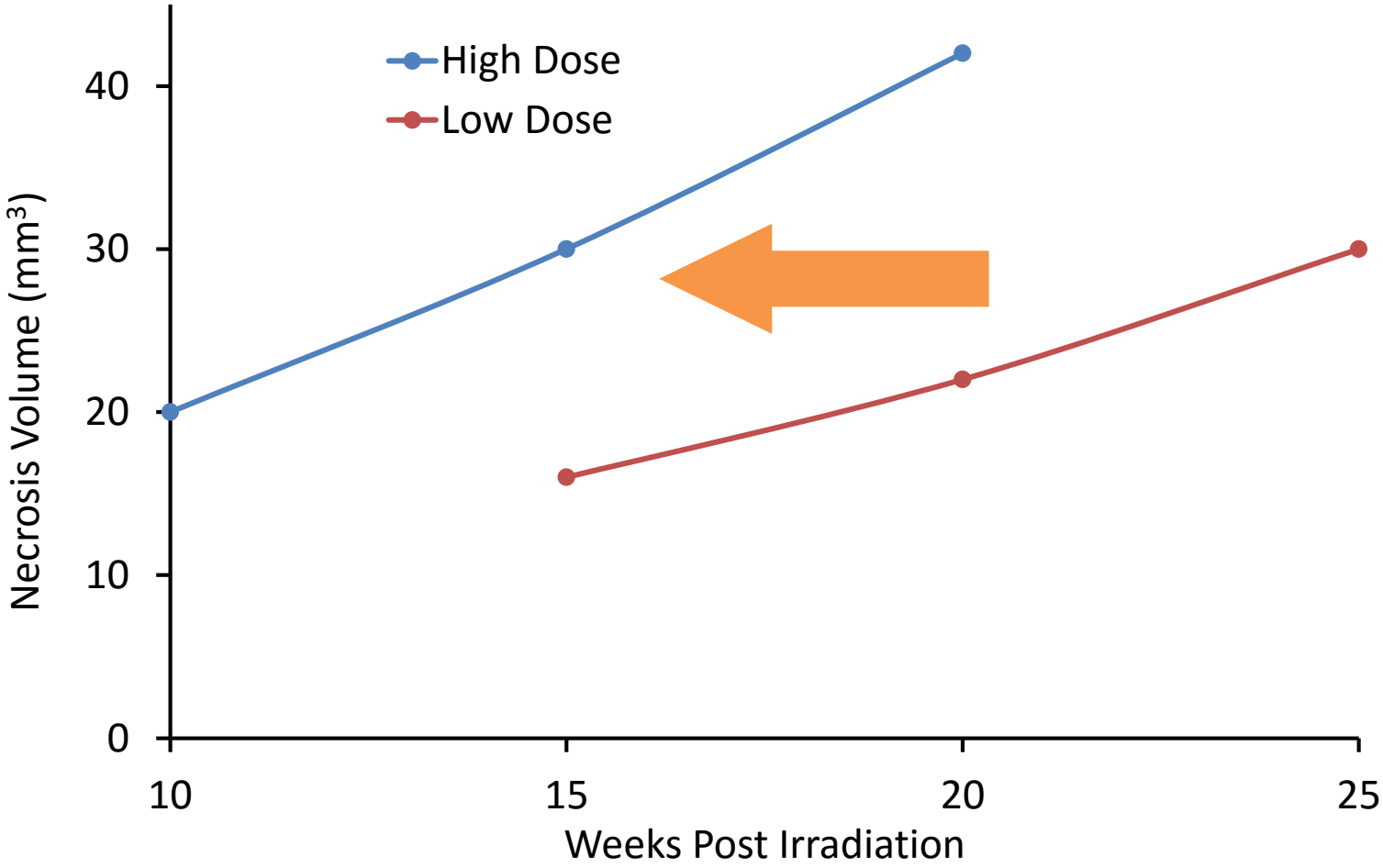
Aim 1: Progression

Identify the relationship between dose to the rate of necrosis progression



Aim 2: Onset

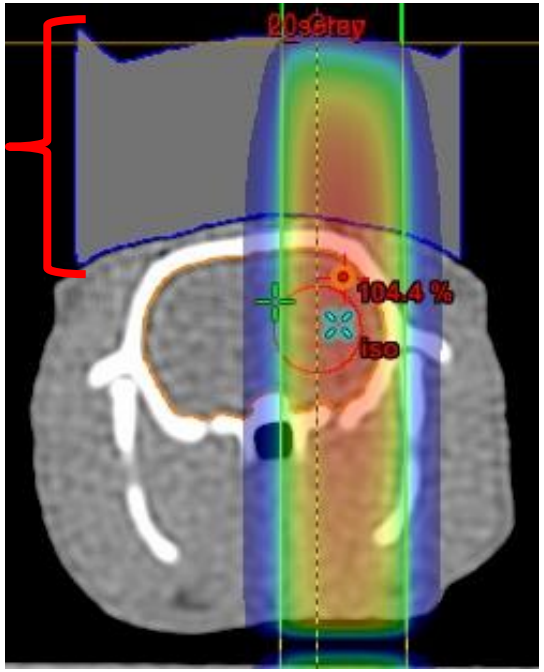
Determine the time to onset of necrosis, relative to dose

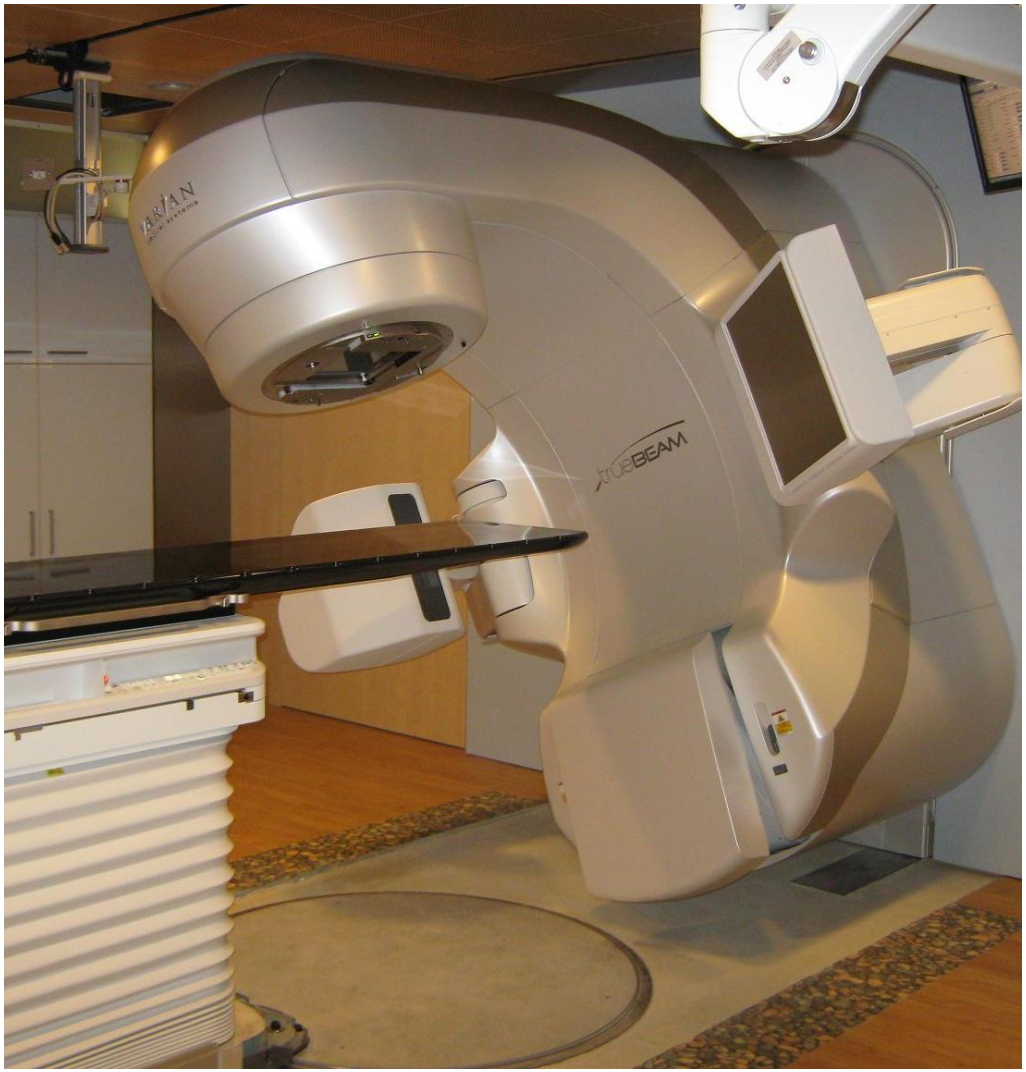


Method: Dosimetry

- 7 Weeks old Fischer 344 Rats
- Varian TrueBeam LINAC
  - Single fraction dose
  - Bolus 1 cm

Bolus



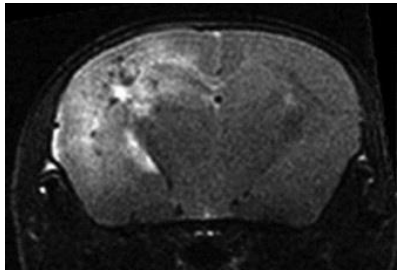


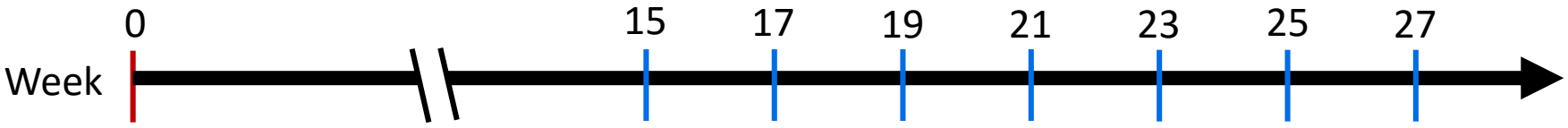
https://maastro.nl/en/3/4/radiotherapy.aspx

Methods: MRI

Healthy rat

Necrosis develops between Week 15-20





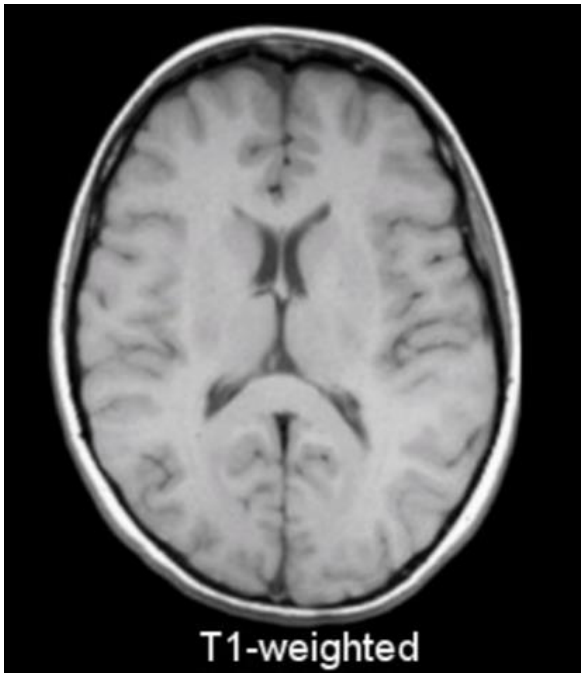
Radiotherapy Treatment

MRI with Gadolinium contrast

Dose (Gy)	Animals
20	3
30	3
40	3
50	3
60	3

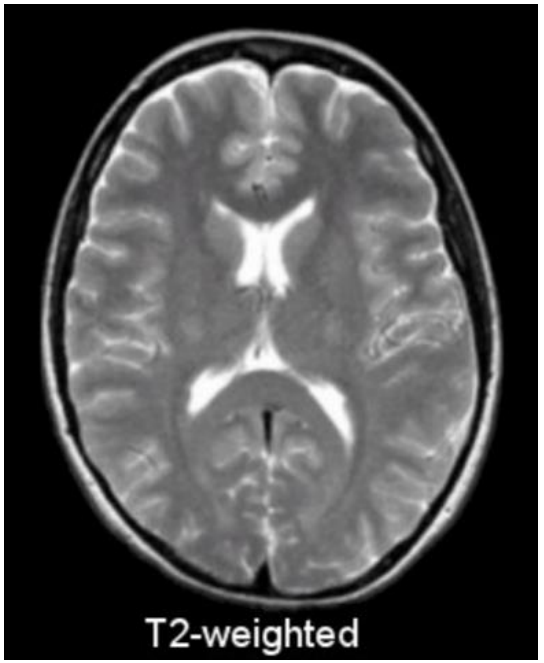
MRI Images

- T1
  - Resting state: longitudinal magnetization
  - Dark Regions: edema, tumor, infarction, necrosis
  - Bright Region: Paramagnetic substances



http://casemed.case.edu/clerkships/neurology/Web%20Neurorad/MRI%20Basics.htm

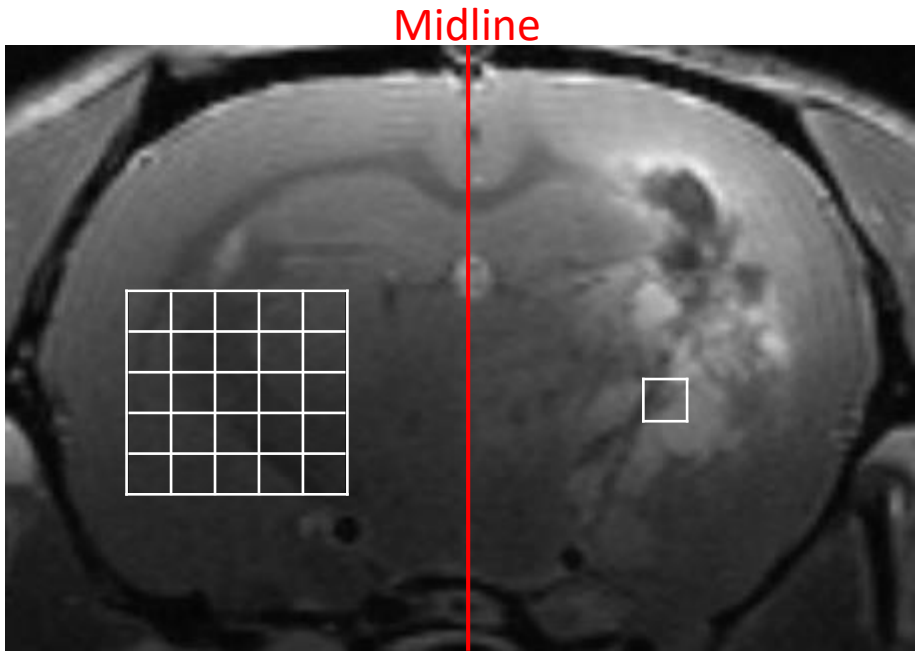
- T2
  - Resting state: transverse magnetization
  - Dark Regions: low proton density, fibrous tissue
  - Bright Region: edema, tumor, infarction



http://casemed.case.edu/clerkships/neurology/Web%20Neurorad/MRI%20Basics.htm

Methods: Image Analysis

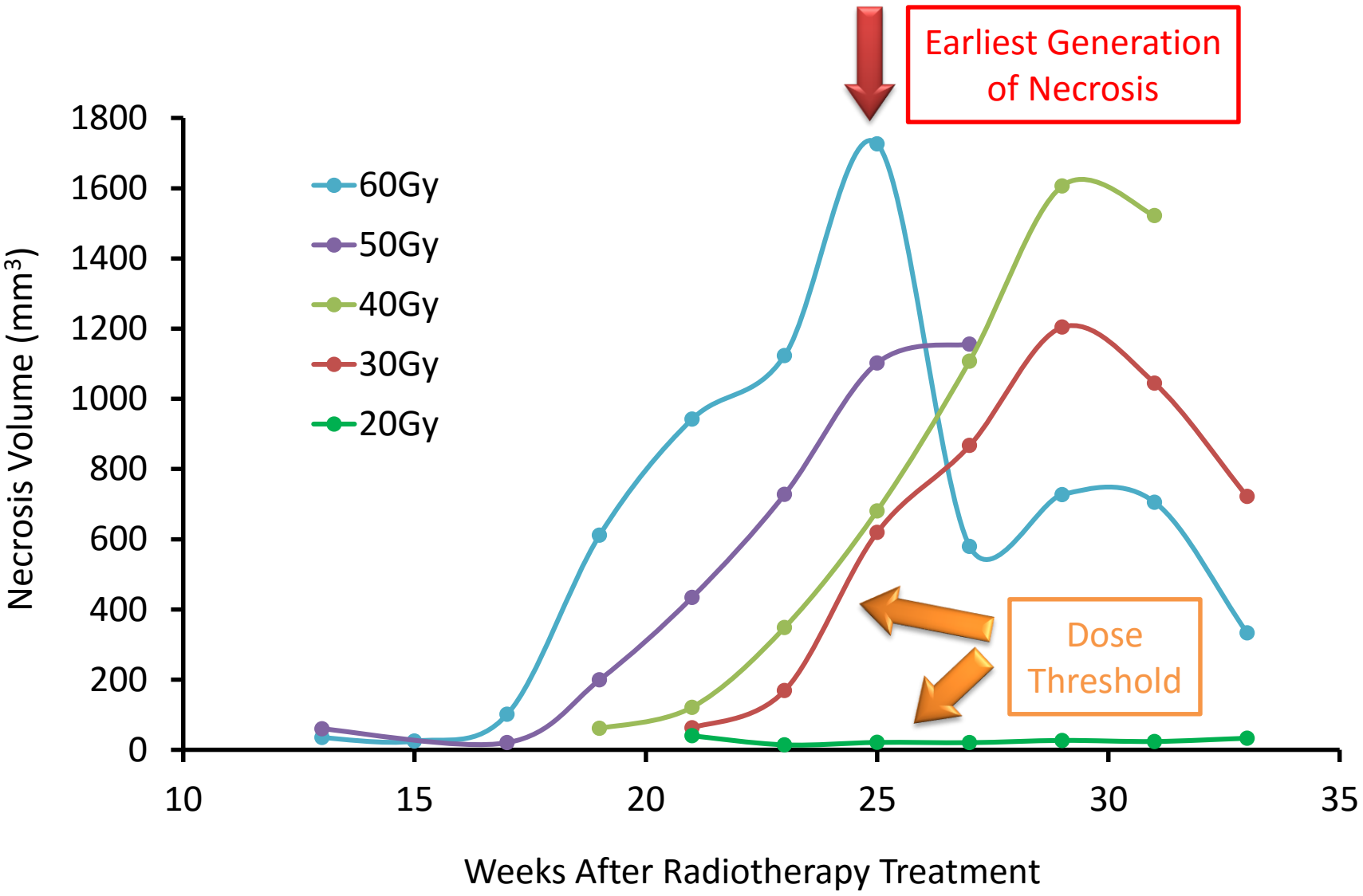
- From the T1 weighted image, the pixel in the right (necrosis) hemisphere is normalized by an average of 25 pixels around its mirror image pixel in the left hemisphere



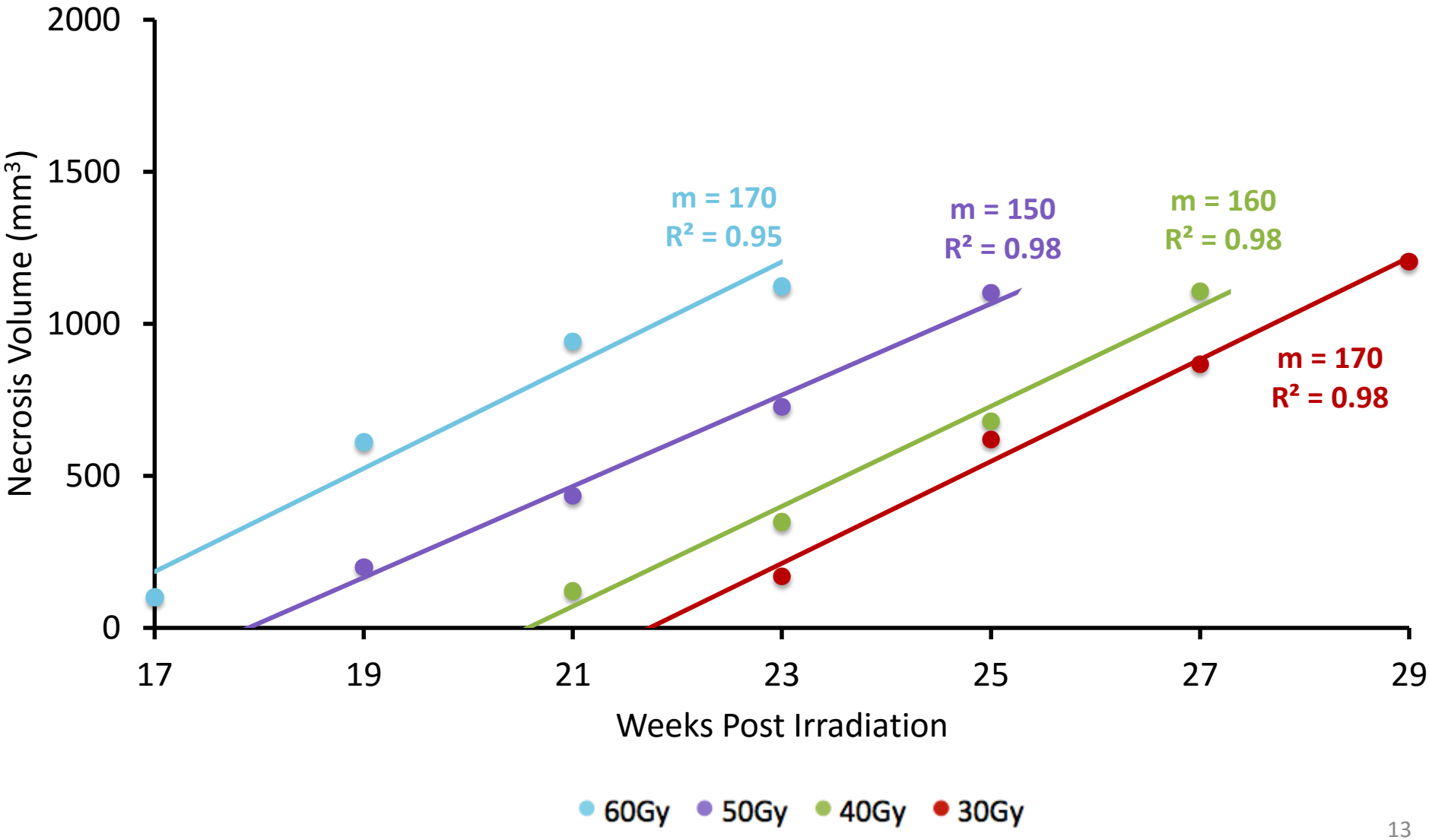
Methods: Determining Necrosis Volume

- Threshold of 1.4 was chosen as the cutoff intensity for normal brain tissue
- The necrotic volume exceeds the threshold

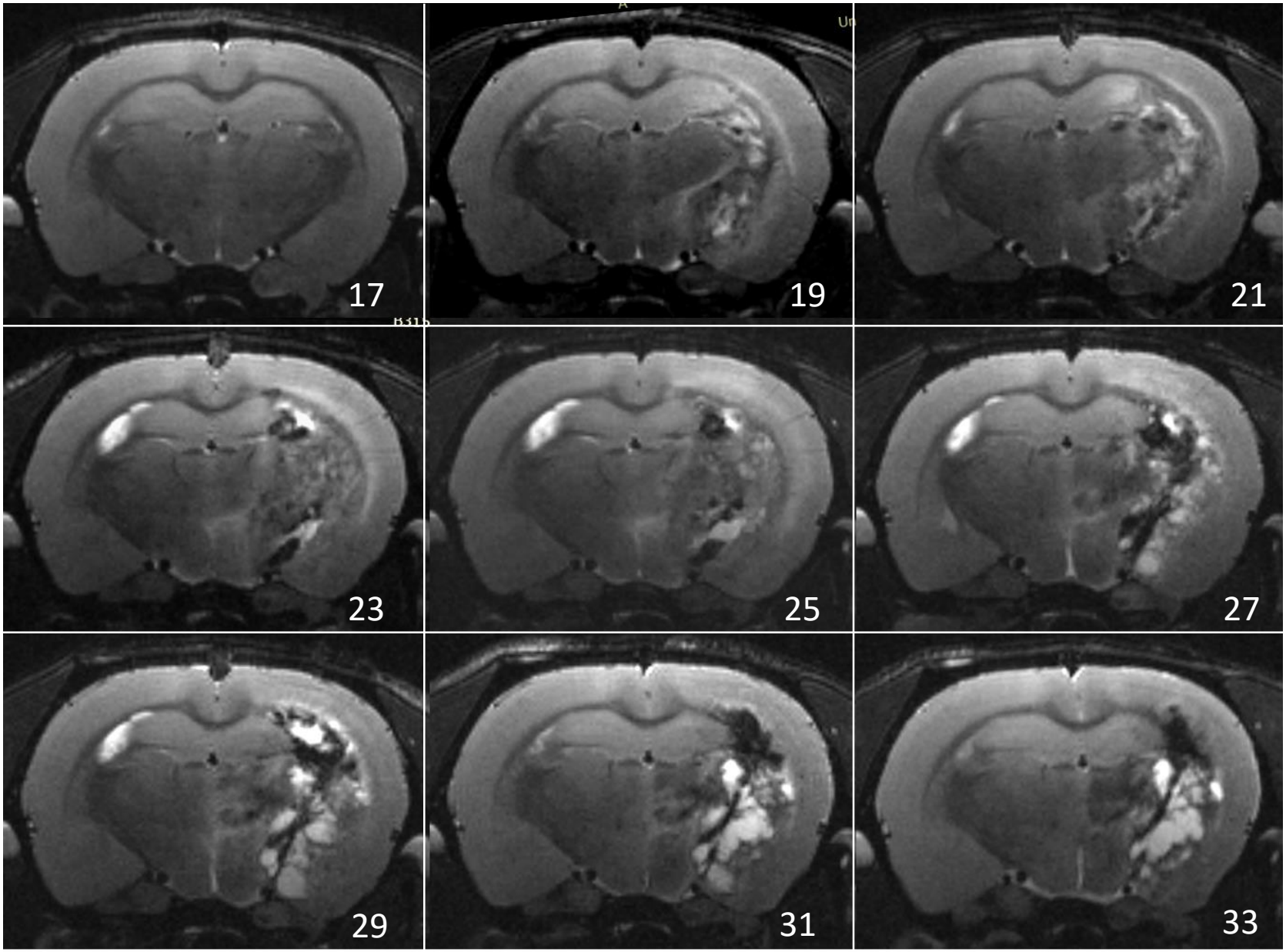
Results: Necrosis Progression



Results: Onset of Necrosis



Results: Other features



Conclusions

- Necrosis progression rate is constant across doses
- Time to necrosis onset is dose dependent
  - Doses less than 30 Gy never generate necrosis
- 60 Gy is a more effective dose

Future

- Applied in large animal study to detect radiation-induced brain necrosis with label-free fluorescence lifetime spectroscopy

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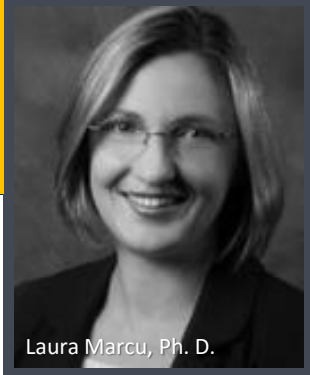
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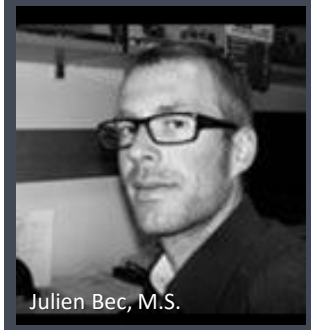
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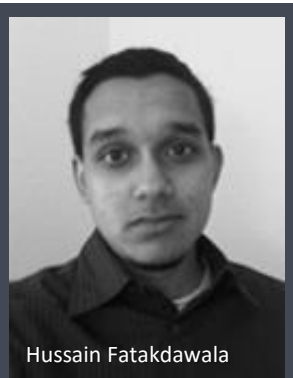
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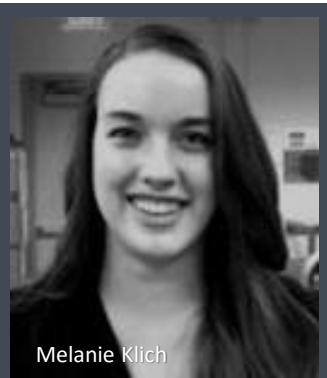
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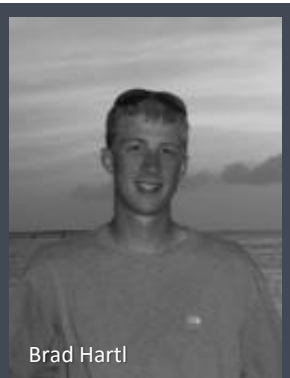
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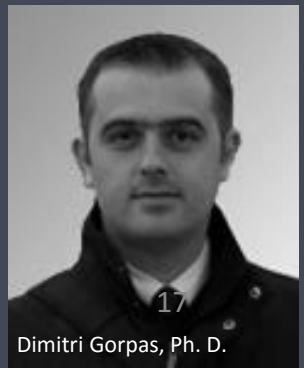
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