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Ultrasound study of Normal Tissue Response to Radiotherapy Treatment

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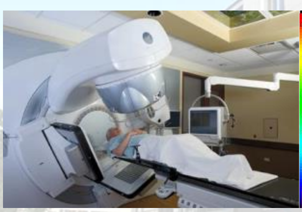
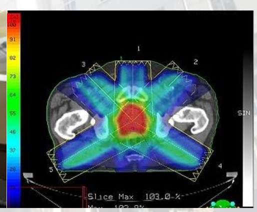
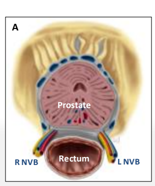
Prostate Radiotherapy





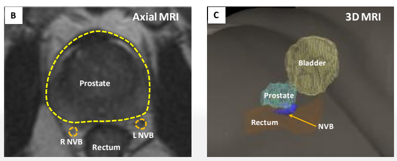
Erectile Dysfunction in Prostate RT

- In the United States, 2.36 million men have survived prostate cancer, and are currently living with cancer-effected life years.
- Erectile dysfunction (ED) is the most common complication of prostate RT.
- The etiology of erectile dysfunction is not unclear. Several studies have reported that neurovascular bundle (NVB) injury is correlated with radiation-associated ED.

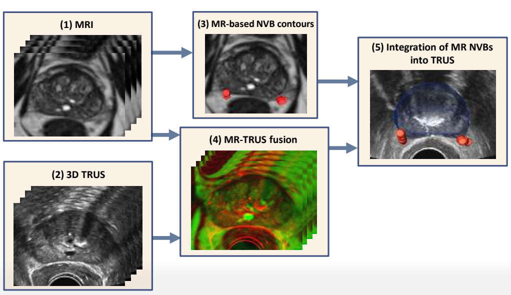


Imaging Technologies

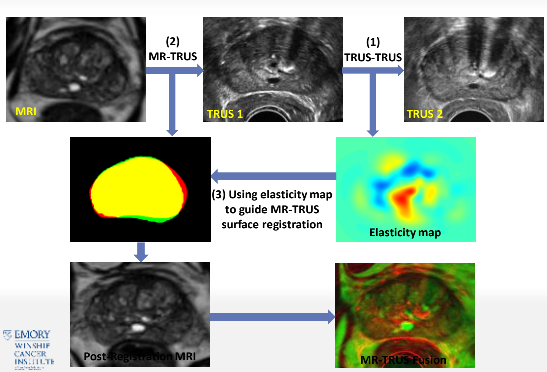
- MRI – accurate target (e.g., dominant tumors, prostate, bladder, NVB, and rectum) delineation
- CT – accurate radiation dose calculation
- Ultrasound – quantitative tissue characterization and Doppler blood flow for treatment response



Multimodality Image Platform

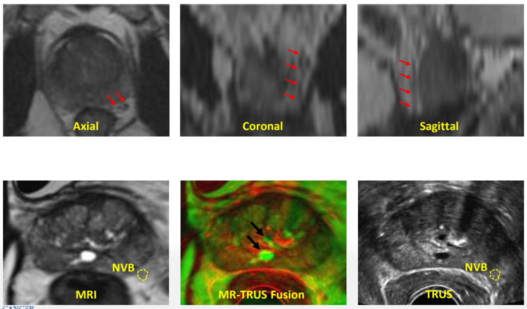


MRI-Ultrasound Registration – Flow Chart

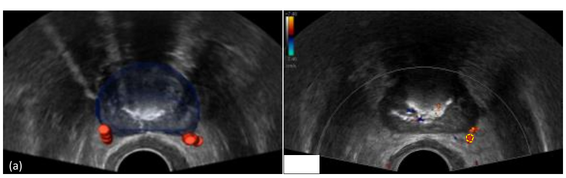


Case Study

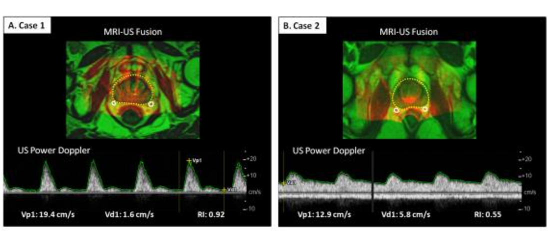
MRI



Case Study (Doppler Ultrasound)



Multimodality Image Platform



PSV – Peak systolic velocity
EDV – End diastolic velocity
RI – Resistive index

Summary

- We have developed a novel approach to improve 3D NVB localization through MR-TRUS fusion for prostate RT, demonstrated its clinical feasibility, and validated its accuracy with ultrasound Doppler data.
- This technique could be a useful tool as we try to spare the NVB in prostate RT, monitor NBV response to RT, and potentially improve post-RT potency outcomes.

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Breast Radiotherapy

Background

3 million are survivors of breast cancer and its treatment. Radiation-induced skin toxicity is the most common side effect of breast cancer radiotherapy impacting 70-100% of patients acutely and as many as 50% of patients in the long term:

Acute	Chronic
Dermatitis	Fibrosis
Erythema	Thickening
Desquamation	Hardening
Hyperpigmentation	Asymmetry
	Disfigurement
	Hypo or hyperpigmentation
	Telangiectasias

Long-Term Treatment Side Effects

- Breast and skin thickening, fibrosis, poor cosmetic outcome
- Behavioral Morbidites:
  - Fatigue
  - Depression
  - Anxiety
  - Stress

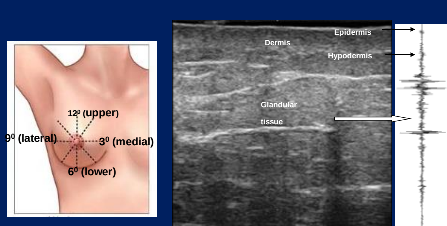
We still cannot reliably predict who will develop short and long-term RT-induced breast and skin toxicity

Why?

- Poorly understood biology

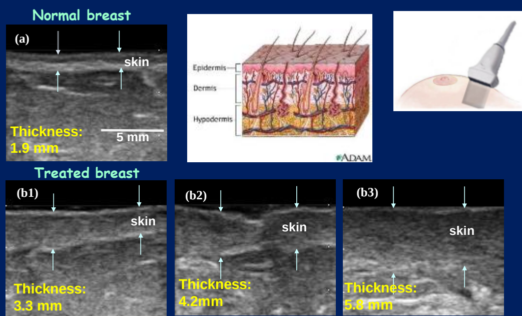
- Lack of objective measures of skin toxicity

Ultrasound Tissue Characterization

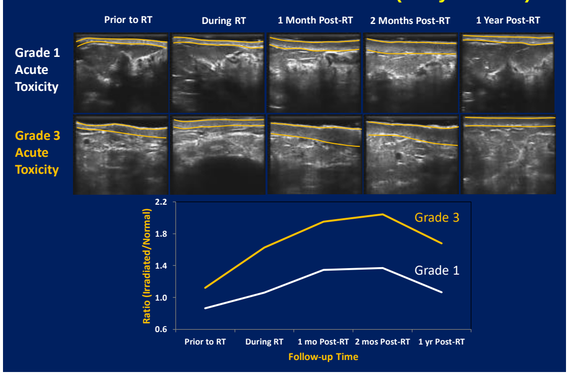


- **Dermal damage - Skin thickness**
- **Hypodermis damage assessment – Pearson correlation coefficient**
- **Glandular tissue – Midband fit**

Skin effects – Irradiated vs. Normal Breast



Clinical Significance of Ultrasound Measurements in Women Treated with Standard XRT (50Gy + boost)



Ultrasound measurement vs. Clinical Assessment

Post-radiation breast-cancer patients

- Thickening of dermis post radiation therapy
- Lowering of Pearson Correlation Coefficient of the irradiated hypodermis
- Increased midband fit - fibrosis

	RTOG 0 (n=5)	RTOG 1 (n=9)	RTOG 2 (n=4)
Skin thickness (mm)	38.4%	23.8%	31.1%
Pearson coefficient	18.4%	35.0%	42.6%
Midband fit	6%	136%*	136%*

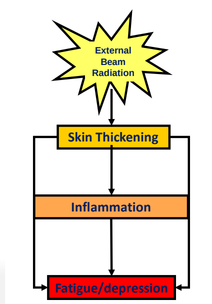
Research Questions

1. Where do breast cancer treatment-related side effects like fatigue and skin toxicity come from? (Inflammation)
2. How do treatment-induced toxicities persist? (Epigenetics)

Working Model and Hypotheses

1) Radiation-induced skin changes may activate the inflammatory response of the body

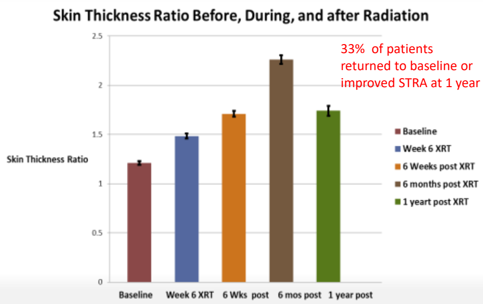
2) Inflammatory proteins are released that can enter the brain and cause fatigue and depression



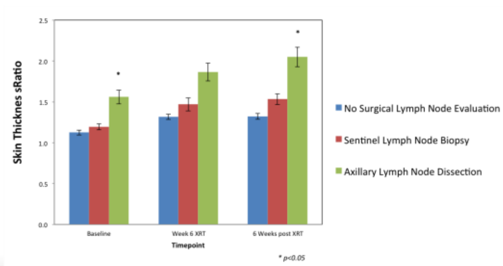
Inflammation is the body's natural response to infection or wounding, but when prolonged or excessive can do damage to many parts of the body including the brain.

Radiation → Tissue damage And Destruction → Activation of NF-kB → Release of Cytokines → Depression Fatigue

Skin Thickness Ratio and XRT



Influence of Lymph Node Surgery on Acute STRA



Torres et al. IJRBP 2015

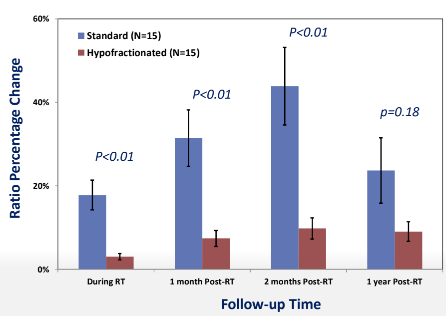
Standard vs Hypofraction Breast RT

Patient Characteristics		Standard RT (N=15)	Hypofractionated RT (N=15)	P-value
Age (years)		61.1 ± 7.5	55.1 ± 11.2	0.09
Race	Caucasian	20 (66.7%)	12 (60.0%)	0.72
	African American	10 (33.3%)	8 (40.0%)	
Chemotherapy	Yes	7 (23.3%)	10 (50.0%)	0.31
	No	23 (76.7%)	10 (50.0%)	
Tumor Stage	Stage 0	8 (26.7%)	5 (25.0%)	0.75
	Stage I	13 (43.3%)	8 (40.0%)	
	Stage II	9 (30.0%)	7 (35.0%)	
Treated Breast	Left Breast	19 (63.3%)	11 (55.0%)	0.87
	Right Breast	11 (36.7%)	9 (45.0%)	

Longitudinal comparison of skin thickness ratio

	Group	Prior to RT	During RT	1 month post-RT	2 months post-RT	1 year post-RT
Standard Group	Control breast (mm)	1.99±0.38	2.03±0.37	1.93±0.38	1.91±0.24	1.87±0.30
	Treated breast (mm)	2.37±0.29	2.81±0.46	3.01±0.70	3.11±0.72	2.52±0.56
	Ratio (Treated/ Control)	1.23	1.41	1.58	1.70	1.45
Hypofractionated Group	Control breast (mm)	2.35±0.42	2.43±0.40	2.35±0.38	2.30±0.34	2.24±0.28
	Treated breast (mm)	2.91±0.71	3.13±0.92	3.16±0.89	3.20±0.71	2.93±0.69
	Ratio (Treated/ Control)	1.24	1.27	1.34	1.39	1.32

Short Course Whole Breast Radiation (Hypofractionation) and STRA



Liu et al. In preparation

Conclusions

- Compared with standard breast RT, hypo-fractionated breast RT resulted in less skin toxicity during and post RT.
- There are complex patient, treatment, physician, and biologic factors associated with skin thickening following radiation treatment making this a difficult problem to study

Implications and Future Directions

- Natural history data of RT-associated skin changes may inform decisions regarding appropriate timing of reconstruction in relationship to radiation
- Is there a relationship between skin thickening and breast asymmetry?
- Biological predictors of poor cosmetic outcomes following radiation are needed

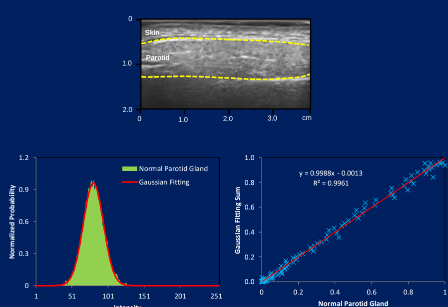
Purpose

- Xerostomia (dry mouth), secondary to parotid-gland injury, is a distressing side-effect in head-and-neck radiotherapy (RT). This study's purpose is to develop a novel ultrasound technique to quantitatively evaluate post-RT parotid-gland injury.
- Recent ultrasound studies have shown that healthy parotid glands exhibit homogeneous echotexture, whereas post-RT parotid glands are often heterogeneous, with multiple hypoechoic (inflammation) or hyperechoic (fibrosis) regions. We propose to use a Gaussian mixture model to analyze the ultrasonic echo-histogram of the parotid glands.

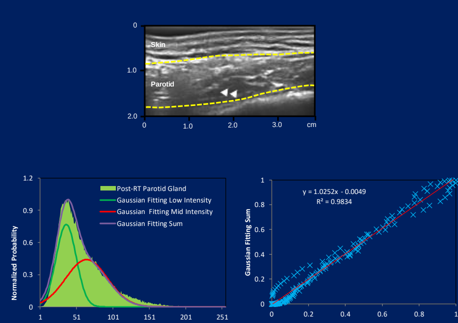
Clinical Study

- All patients experienced RTOG grade 1 or 2 salivary-gland toxicity. (1) control-group: 13 healthy-volunteers, served as the control; (2) acute-toxicity group - 20 patients (mean age: 62.5 ± 8.9 years, follow-up: 2.0±0.8 months); and (3) late-toxicity group - 18 patients (mean age: 60.7 ± 7.3 years, follow-up: 20.1±10.4 months).
- Each participant underwent an ultrasound scan (10 MHz) of the bilateral parotid glands
- An echo-intensity histogram was derived for each parotid and a Gaussian mixture model was used to fit the histogram using expectation maximization (EM) algorithm. The quality of the fitting was evaluated with the R-squared value.

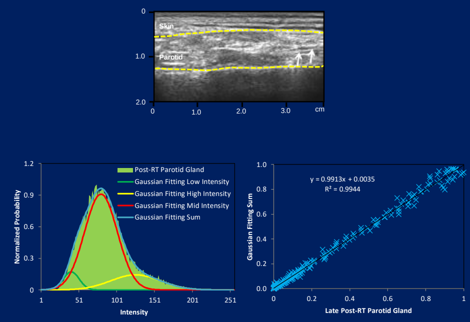
Case Study Result - Normal



Case Study Result - Acute



Case Study Result - Late



Results – Three Group

Results

- (1) Control-group: all parotid glands fitted well with one Gaussian component, with a mean intensity of 79.8±4.9 (R-squared>0.96).
- (2) Acute-toxicity group: 37 of the 40 post-RT parotid glands fitted well with two Gaussian components, with a mean intensity of 42.9±7.4, 73.3±12.2 (R-squared>0.95).
- (3) Late-toxicity group: 32 of the 36 post-RT parotid glands fitted well with 3 Gaussian components, with mean intensities of 49.7±7.6, 77.2±8.7, and 118.6±11.8 (R-squared>0.98).

Implications and Future Directions

- This work has demonstrated that the Gaussian mixture model of the echo-histogram could quantify acute and late toxicity of the parotid glands.
- This study provides meaningful preliminary data from future observational and interventional clinical research.

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Thank you!

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