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THE UTSW EXPERIENCE: ULTRA-HYPOFRACTIONATED PARTIAL BREAST RADIOTHERAPY

ASAL RAHIMI M.D., MS

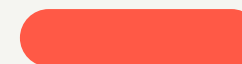
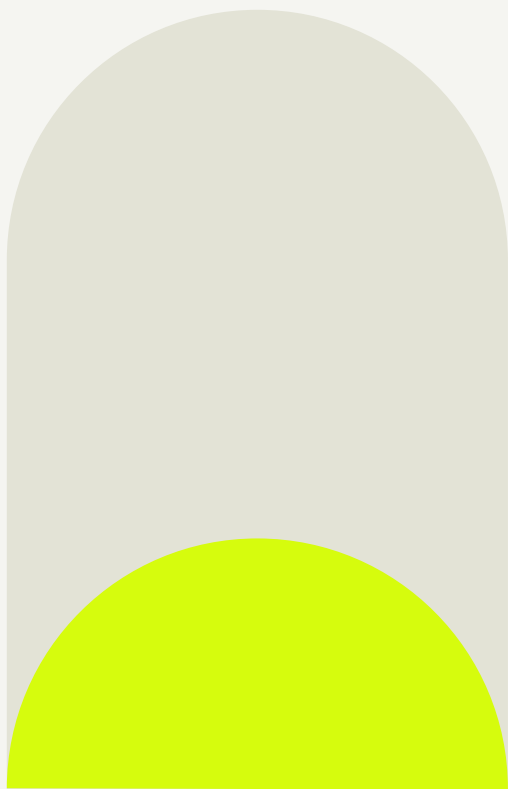
ASSOCIATE PROFESSOR AND VICE CHAIR OF DEI

CHIEF OF BREAST RADIATION

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DISCLOSURES:

- Employee of University of Texas Southwestern Medical Center
- Speaking Honoraria: Accuray and Hologic
- Research grants: Accuray (5 fraction and 1 fraction S-PBI trials)
- Scientific Advisory Boards: Hologic, GE Health

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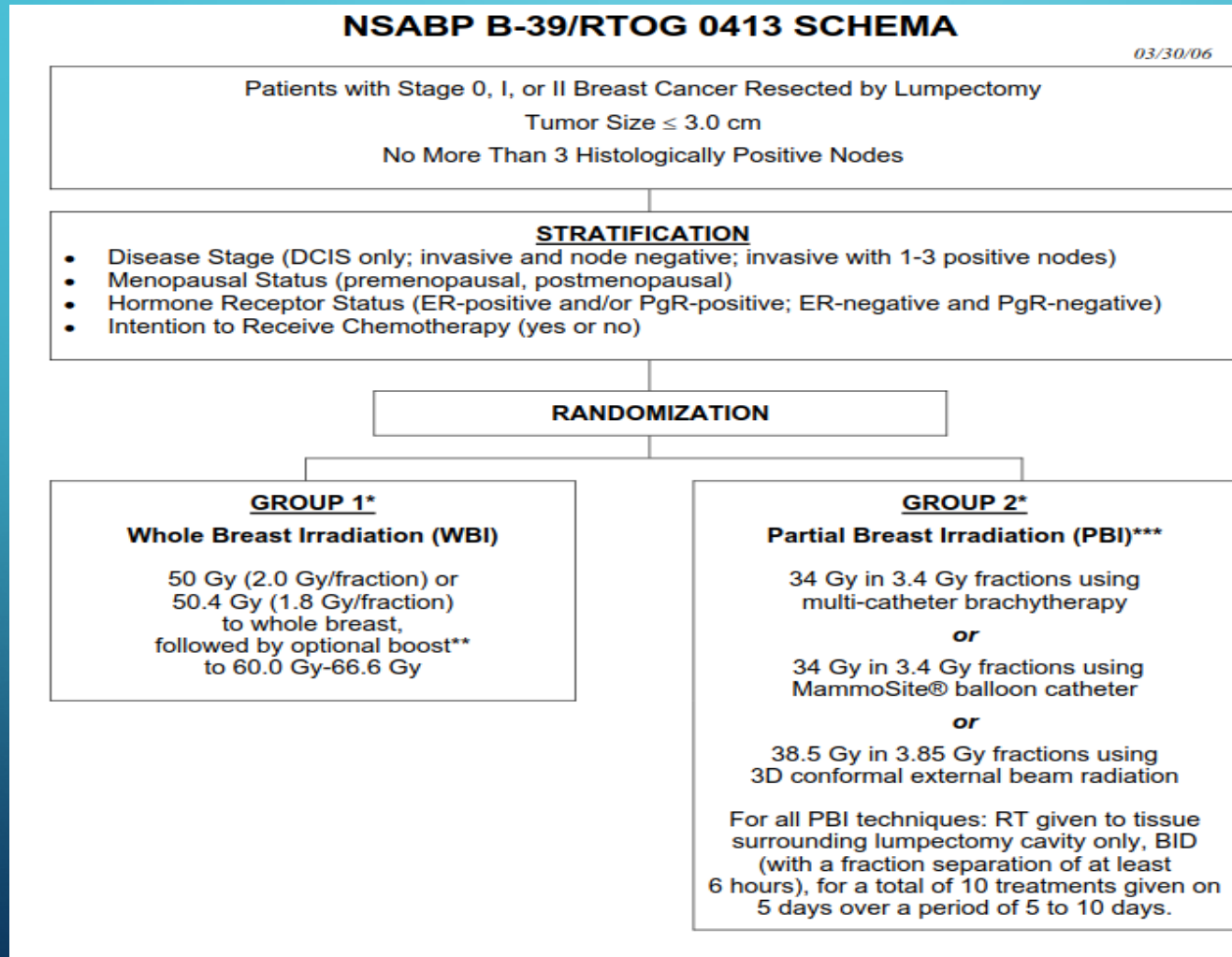
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NSABP-39/RTOG 0413(NRG): RANDOMIZED PHASE III STUDY OF WBI VS PBI FOR WOMEN WITH STAGE 0,I, OR II BREAST CANCER



NSABP 39 CONCLUSIONS:

- Statistical analysis cannot declare WBI & PBI are equivalent in ipsilateral local breast tumor recurrence. Absolute difference at 10 years is only 0.7% favoring WBI
- Recurrence free interval higher for WBI (SS) v PBI, but absolute difference only 1.6%
- DDFI, OS, DFS were not SS for PBI v WBI
- PBI may still be an acceptable alternative to WBI for early stage breast cancer as IBTR and RFI differences are so small

NSABP-39 COSMESIS OUTCOMES

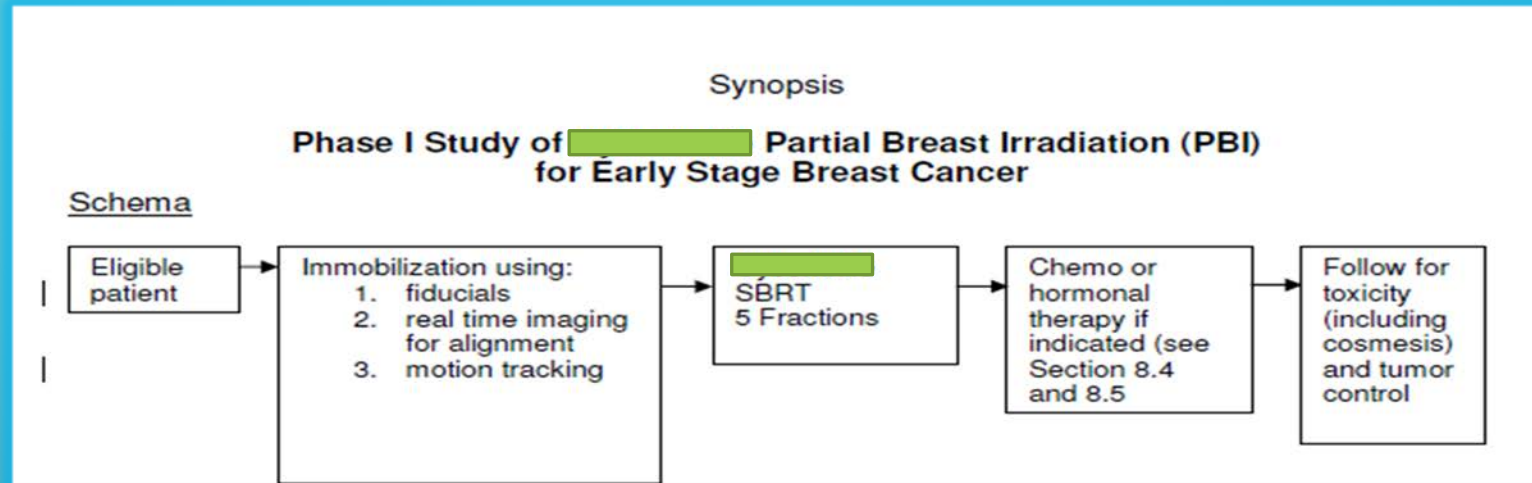
- Pts stratified by chemo use, and assessed on 4 point scale by patients, MD, and digital photos (3 teams of physicians) at baseline and 3 years
- 900 analyzable pts ; 420 chemo patients and 480 no chemo pts
 - Chemo pts: PBI **equivalent** to WBI on **patient assessment**
 - Chemo pts: **PBI worse** than WBI on **MD assessment**
 - Pts with No Chemo: PBI **equivalent** to WBI on **patient assessment**
 - Pts with No Chemo: **PBI worse** than WBI on **MD assessment**
 - Chemo pts: **PBI worse** than WBI when assessed by **digital photos**
 - Pts with No chemo: **WBI worse** than PBI when assessed by **digital photos**
- **Conclusion:** Pt rated cosmetic outcome, based on Global cosmetic scale and satisfaction were equivalent for PBI and WBI.
- PBI resulted in worse cosmetic outcome on MD rating.
- On DP central review, cosmetic outcome is worse for PBI in Chemo treated group and worse for WBI in the no-Chemo group.

STEREOTACTIC PARTIAL BREAST RADIATION (S-PBI)

ADVANTAGES OF SBRT PBI VS. PBI BRACHYTHERAPY

- Non-invasive
- More convenient
- Less risk of infection
- Able to minimize PTV margins in comparison to 3D PBI (3D-PBI has 2.5 cm margins vs 1.5 cm)

UTSW 5 fraction Early Stage Breast Cancer Stereotactic-PBI Trial Schema:

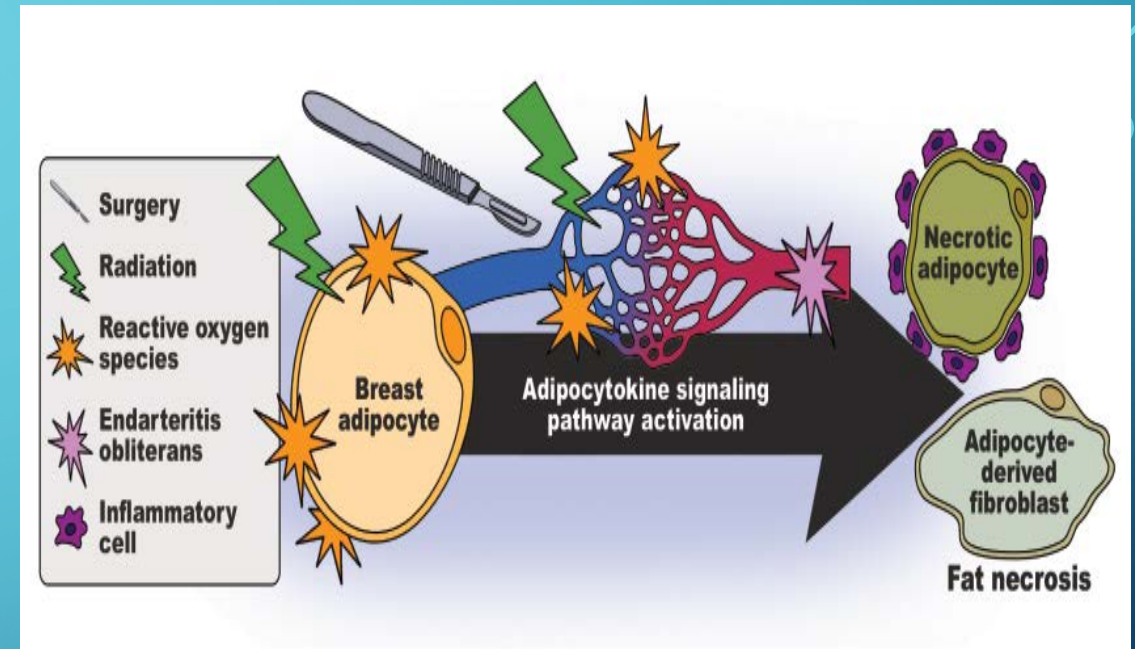


Dose Escalation:

<u>Step</u>	<u>No. Fractions</u>	<u>Dose per fraction (Gy)</u>	<u>Total Dose (Gy)</u>	<u>No. Patients</u>
-1	5	5.5	27.5	7-15
0 (starting)	5	6	30.0	7-15
1	5	6.5	32.5	7-15
2	5	7	35.0	7-15
3	5	7.5	37.5	7-15
4	5	8	40	7-15

TREATMENT VOLUME MATTERS FOR S-PBI!!

- 11 patients developed palpable fat necrosis (4 of which were symptomatic)
- Median time to development of fat necrosis was 12.7 months
- 5/11 pts with fat necrosis in 37.5 Gy arm (cohort with largest PTVs)
- ROC curve analyses showed **PTV >99.5cc** had highest predicted probability of fat necrosis (p=0.01)



Hypothesized mechanism for fat necrosis

Risk Factors for Fat Necrosis after Stereotactic Partial Breast Irradiation (S-PBI) for Early Stage Breast Cancer in a Phase I Clinical Trial- ASTRO 2019.
A. S. Rahimi¹, Y. Zhang¹, F. Hossain¹, A. E. Spangler¹, D. N. Kim¹, M. Leitch¹, R. Wooldridge¹, C. Ahn², B. Zhao¹, B. Haley¹, R. Rao³, A. Rivers⁴, X. Gu¹,
and R. D. Timmerman⁵

MULTIVARIATE ANALYSES FOR FACTORS ASSOCIATED WITH ANY FAT NECROSIS A) AND PAINFUL FAT NECROSIS B)

A- Any Fat Necrosis

Parameter	cc	Odds Ratio Estimate	95% C.I. for Odds Ratio	P-Value
Ipsi Breast volume (cc)	1062.7	1.001	(1.001,1.002)	0.007

B) Painful Fat Necrosis

Parameter	Odds Ratio Estimate	95% C.I. for Odds Ratio	P-value
Two Fractions <24 Hours	13.163	(1.0121,171.1984)	0.049
V45.0Gy (cc)	1.069	(1.0201,1.1197)	0.005

Risk Factors for Fat Necrosis after Stereotactic Partial Breast Irradiation (S-PBI) for Early Stage Breast Cancer in a Phase I Clinical Trial- ASTRO 2019

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FAT NECROSIS DOSE CONSTRAINTS FOR 5-FRXN S-PBI

Table 4. Dose constraint recommendations for stereotactic partial breast irradiation to prevent painful necrosis in patients with breast volume greater than 1000 cm³*

Factor	Constraint
Maximal dose	48 Gy
V37.5	95 cm ³
V40 Gy	85 cm ³
V42.5 Gy	50 cm ³
V45 Gy	20 cm ³
V47.5 Gy	1 cm ³
Planning target volume	<100 cm ³

*

Only one patient with breast volume less than 1000 cm³ developed fat necrosis, and she was not included in calculation of predictive dose-constraints.

Clinical Investigation

Cosmetic Outcomes of a Phase 1 Dose Escalation Study of 5-Fraction Stereotactic Partial Breast Irradiation for Early Stage Breast Cancer



Asal Rahimi, MD, MS,^{*} Howard E. Morgan, MD,^{*}
Dong W. Kim, MD, PhD,^{*} Yuanyuan Zhang, MD, PhD,^{*}
Marilyn Leitch, MD,[†] Rachel Wooldridge, MD,[†] Sally Goudreau, MD,[‡]
Barbara Haley, MD,[§] Roshni Rao, MD,^{||} Aisha Rivers, MD,[¶]
Ann E. Spangler, MD,^{*} Ryan T. Jones, MD,[#] Stella Stevenson, BSRT(T),^{*}
Jason Staley, SBRT(R)(T),^{*} Kevin Albuquerque, MD,^{*}
Chul Ahn, PhD,^{**} Sarah Neufeld, BS, MS,^{*}
Prasanna G. Alluri, MD, PhD,^{*} Chuxiong Ding, PhD,^{*}
Dan Garwood, MD,^{*} Stephen Seiler, MD,[‡] Bo Zhao, PhD,^{††}
Xuejun Gu, PhD,^{*} and Robert Timmerman, MD^{*}

Departments of ^{}Radiation Oncology, [†]Surgery, [‡]Radiology, [§]Medicine, Division of Hematology-Oncology, University of Texas Southwestern Medical Center, Dallas, Texas; ^{||}Department of Surgery, Columbia University, New York, New York; [¶]Department of Surgery, Memorial Health Care System, Pembroke Pines, Florida; [#]Department of Radiation Oncology, Tennessee Oncology, Nashville, Tennessee; ^{**}Department of Population and Data Sciences, University of Texas Southwestern Medical Center, Dallas, Texas; and ^{††}Department of Medical Physics, Memorial Sloan Kettering Cancer Center, Uniondale, New York*

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• Patient Reported Cosmesis Outcomes on 5 fraction CyberKnife Trial

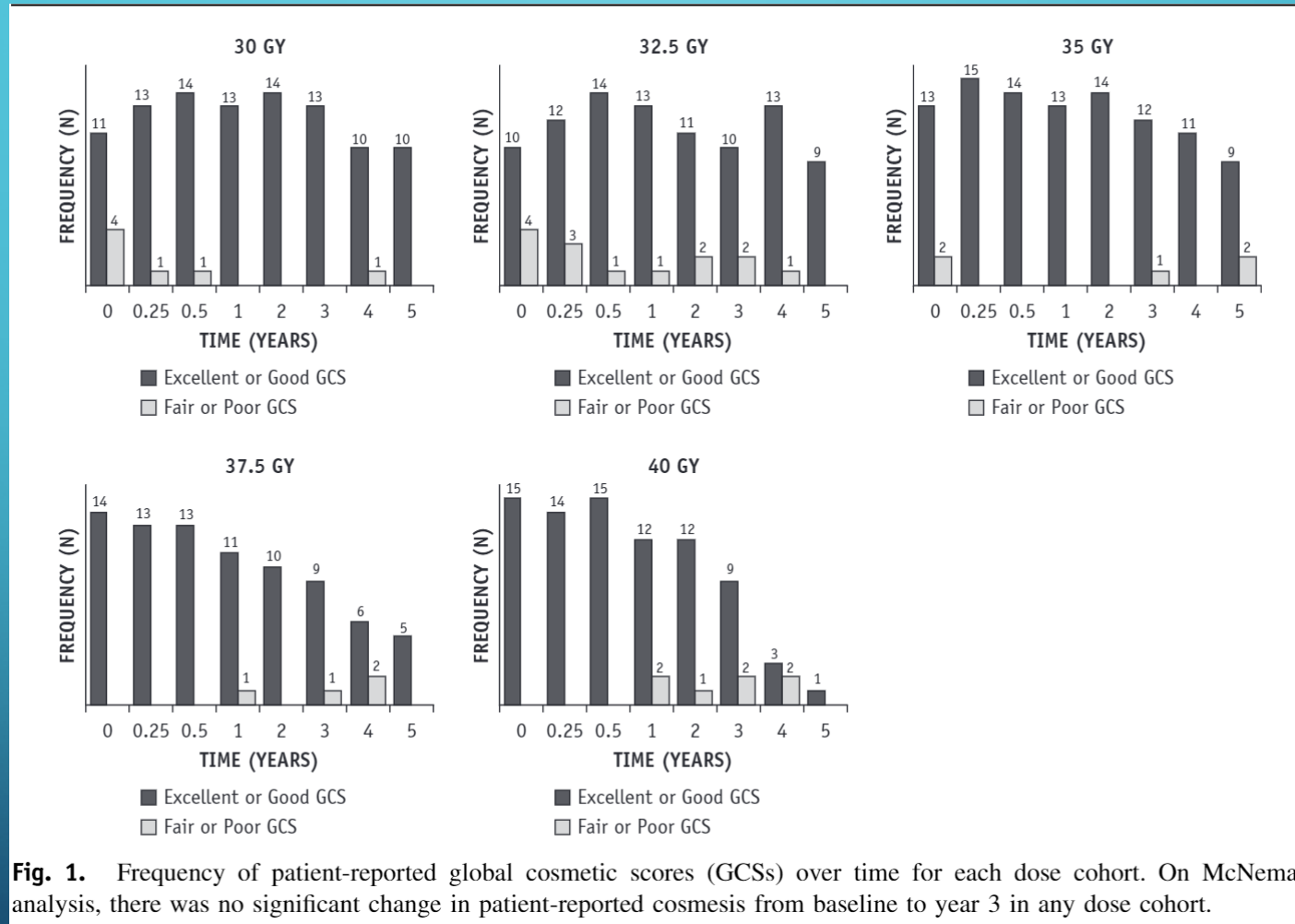
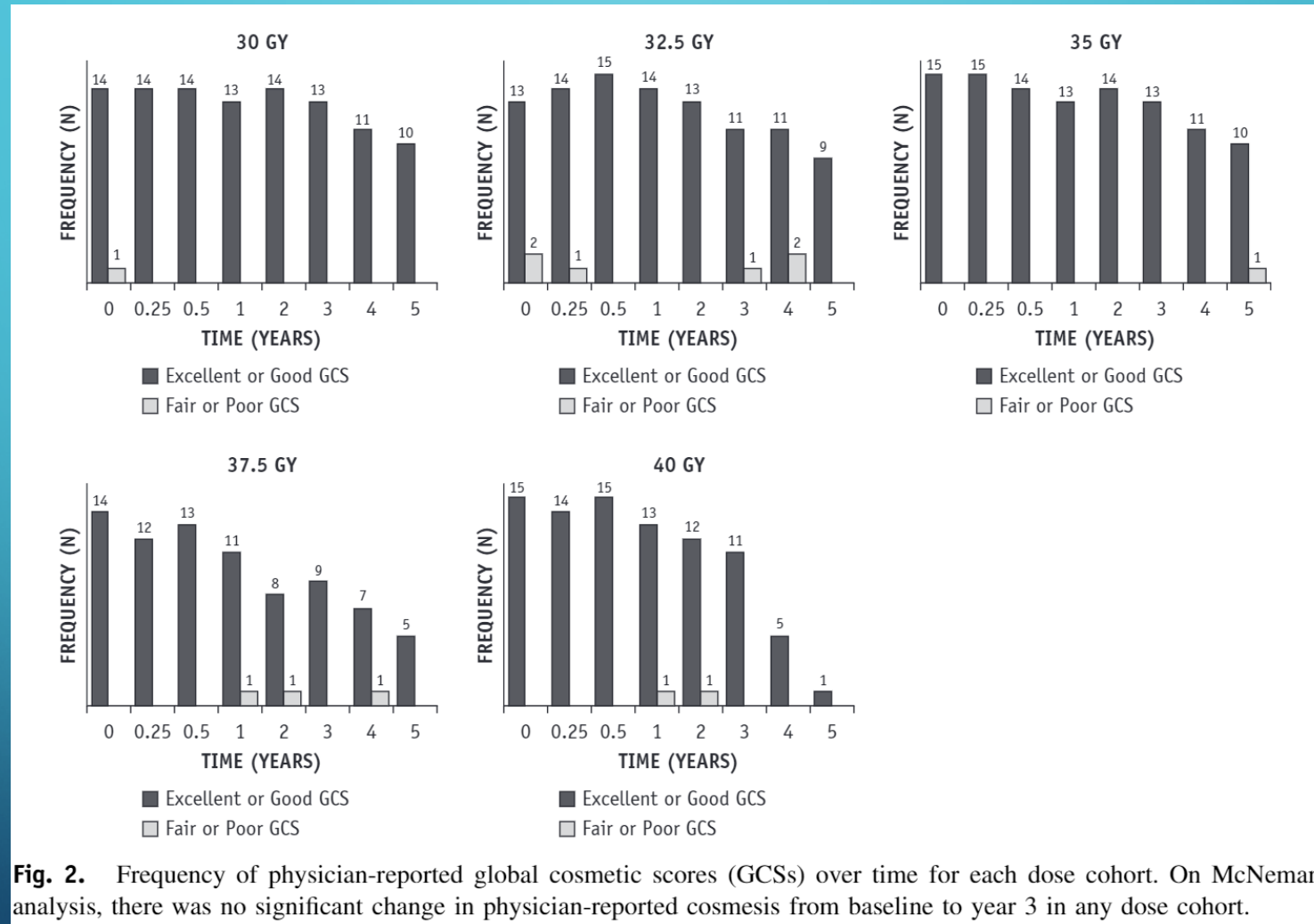


Fig. 1. Frequency of patient-reported global cosmetic scores (GCSs) over time for each dose cohort. On McNemar analysis, there was no significant change in patient-reported cosmesis from baseline to year 3 in any dose cohort.

Physician Reported Cosmesis Outcomes on 5 fraction CyberKnife Trial



Independent Physician Panel Reported Cosmesis Outcomes on 5 fraction CyberKnife Trial

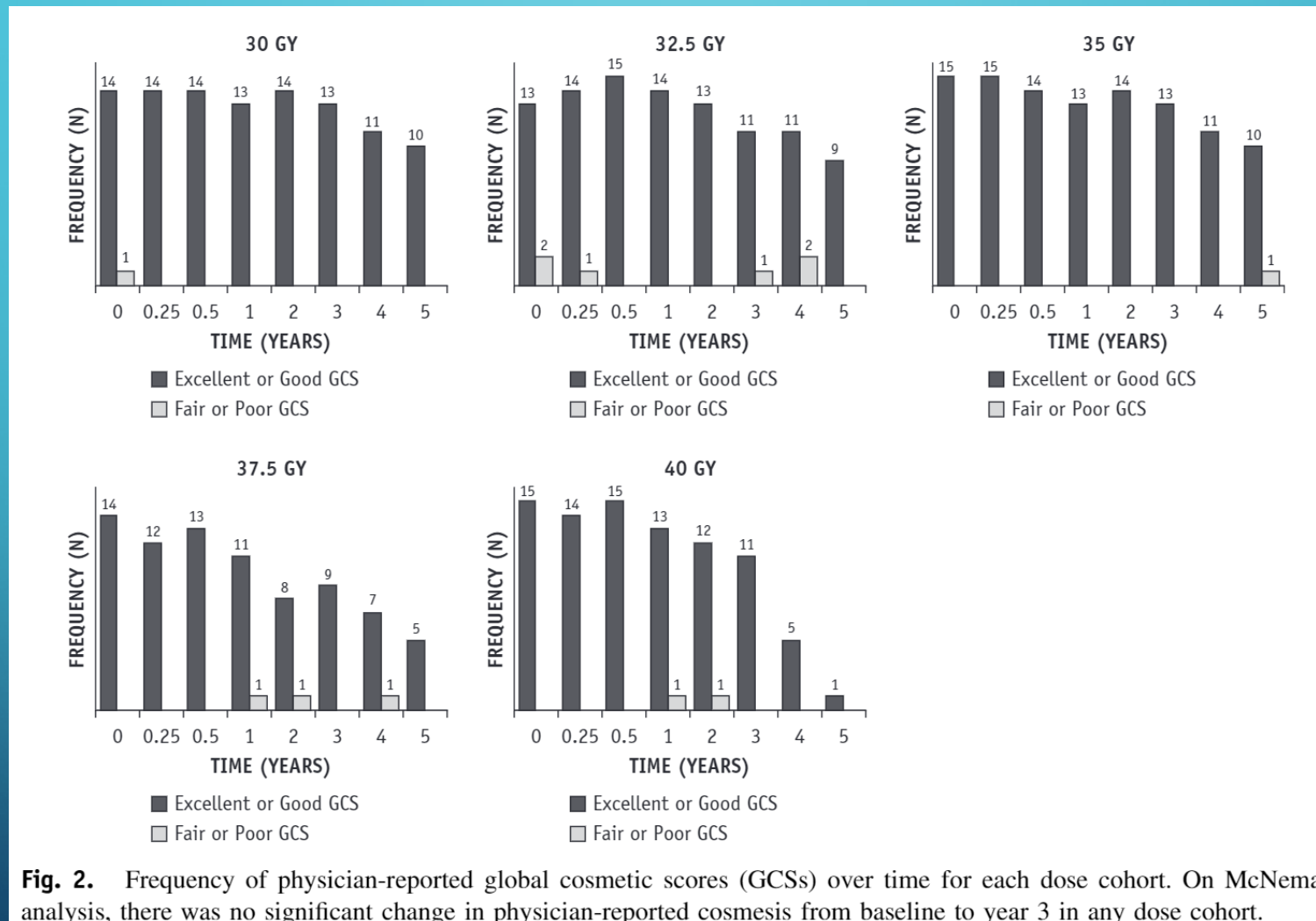


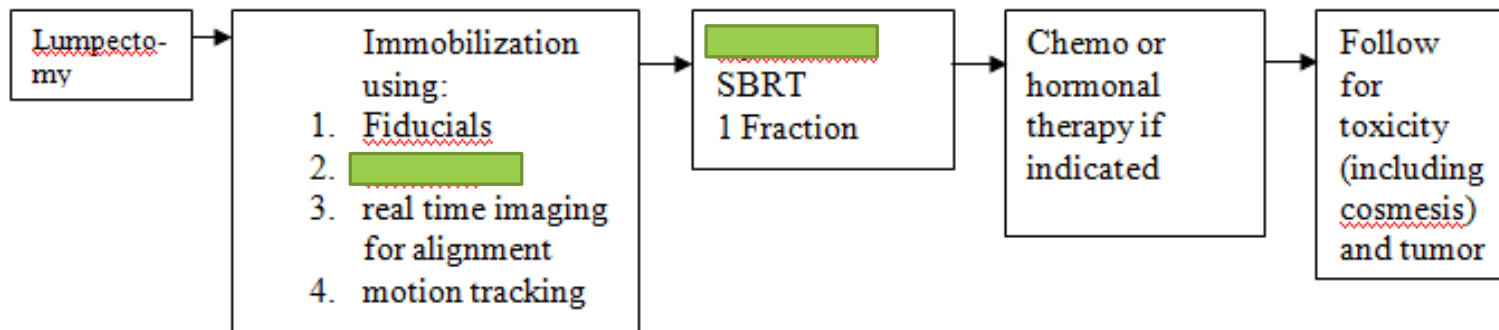
Fig. 2. Frequency of physician-reported global cosmetic scores (GCSs) over time for each dose cohort. On McNemar analysis, there was no significant change in physician-reported cosmesis from baseline to year 3 in any dose cohort.

***Can We Mimic and/or improve 1 Fraction
Intra-Operative Breast Radiation with S-PBI?***

UTSW PHASE I TRIAL- 1 FRACTION ADJUVANT S-PBI:

Phase I Study of [REDACTED] Partial Breast Irradiation (PBI) for Early Stage Breast Cancer

Schema



<u>Step</u>	<u>No. Fractions</u>	<u>Dose per fraction [1]</u>	<u>No. Patients</u>
-1	1	20	7-15
0 (starting)	1	22.5	7-15
1	1	26.5	7-15
2	1	30	7-15

UTSW PHASE I TRIAL- 1 FRACTION ADJUVANT S-PBI:

Results: From June 2016 to January 2021, 11, 8, and 10 patients were treated to doses of 22.5, 26.5, or 30 Gy in a single fraction, respectively, with median follow-up being 47.9, 25.1, and 16.2 months. No patients experienced acute (<90 days) grade 3 or higher treatment-related toxicity, and maximum tolerated dose was not reached. There were 2 delayed grade 3 toxicities. Four patients (13.8%) developed fat necrosis across all 3 cohorts, which compares favorably with results from other PBI trials.

[Preliminary Results of Multi-Institutional Phase 1 Dose Escalation Trial Using Single-Fraction Stereotactic Partial Breast Irradiation for Early Stage Breast Cancer](#)

Rahimi, A., Simmons A., Kim D.N., Leitch M., Haas J., Gu X., Ahn C., Ga, A., Spangler A., Morgan H.E., Gaudreau, S., Sellar, S., Farr, D., Wooldridge R., Haley B., Bahrami, S., Neufeld S., Mendez, C., Alluri P., Rao R. and Timmerman, R.D.

International Journal of Radiation Oncology Biology Physics • 1 March 2022

UTSW PHASE I TRIAL- 1 FRACTION ADJUVANT S-PBI:

Table 5 Frequency of EG GCS by patient and physician report

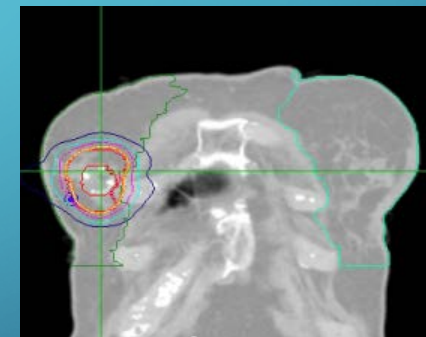
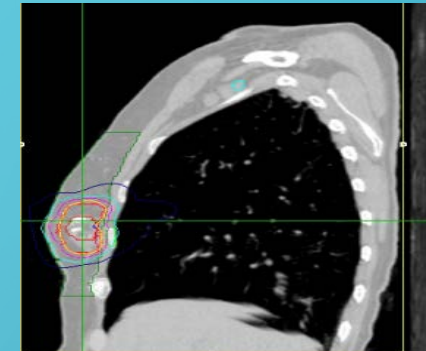
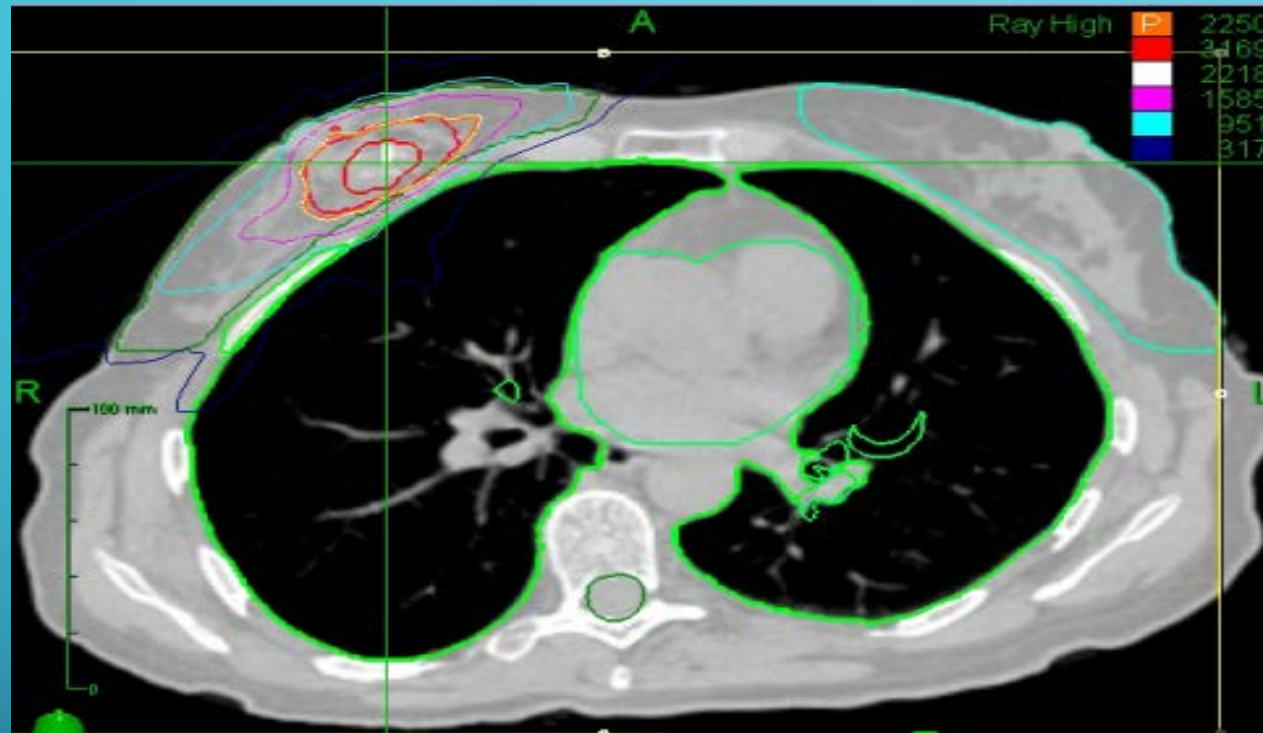
Cohort	Patient-rated EG cosmesis			Physician-rated EG cosmesis		
	Baseline	Month 12	Month 24	Baseline	Month 12	Month 24
22.5 Gy	91% (10/11)	90% (9/10)	90% (9/10)	100% (11/11)	100% (10/10)	100% (10/10)
26.5 Gy	88.9% (8/9)	87.5% (7/8)	100% (8/8)	100% (9/9)	87.5% (7/8)	87.5% (7/8)
30 Gy	80% (8/10)	75% (6/8)	-	90% (9/10)	100% (8/8)	-
Total	92.9% (26/30)	84.6% (22/26)	94.4% (17/18)	96.7% (29/30)	96.2% (25/26)	94.4% (7/18)

Abbreviations: EG = excellent/good; GCS = global cosmetic scores.

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TREATMENT

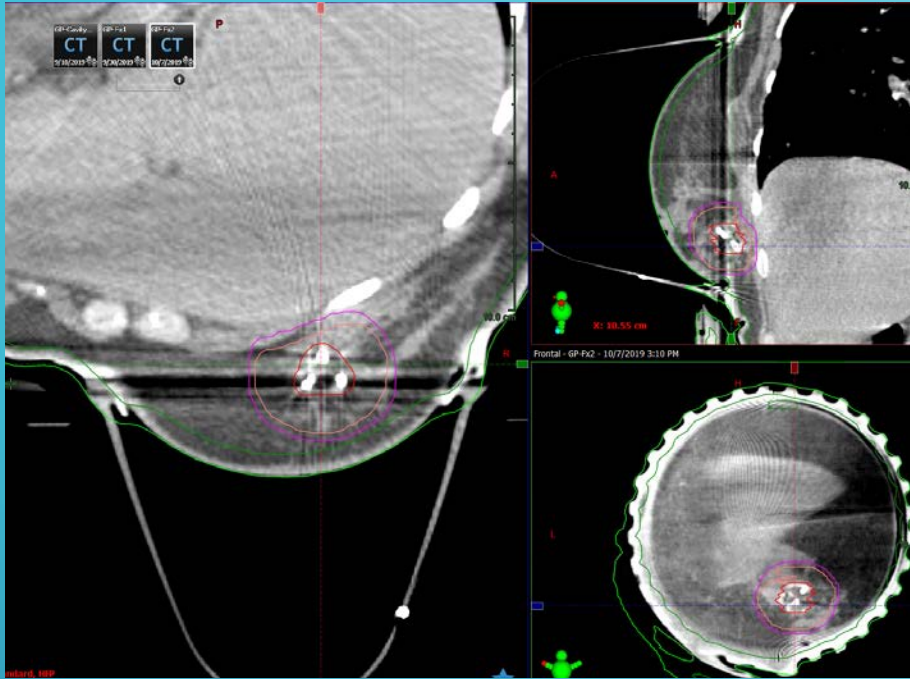


Dose 22.5 Gy in 1 Fraction

CTV= lumpectomy cavity +10mm

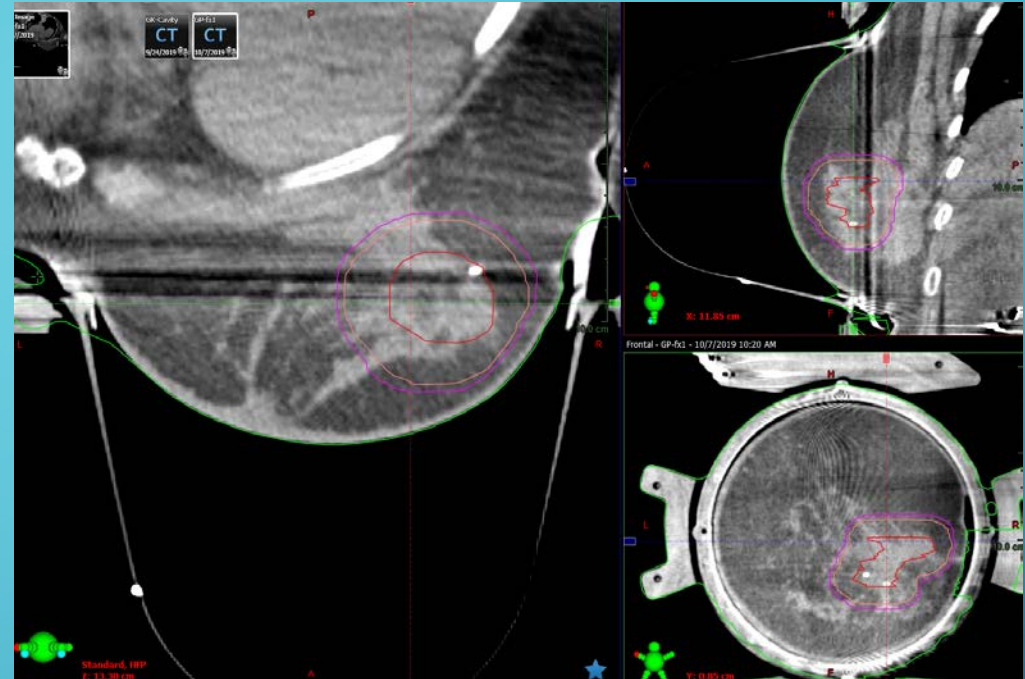
(5 mm off skin, and off of lung-chest wall interface)

CTV: 27.6 cc ; Device 2 x2 cm



Device= 2x2cm

GTV=5 cc
 CTV=37 cc
 PTV=56.8 cc



No device; cavity more difficult to discern and larger

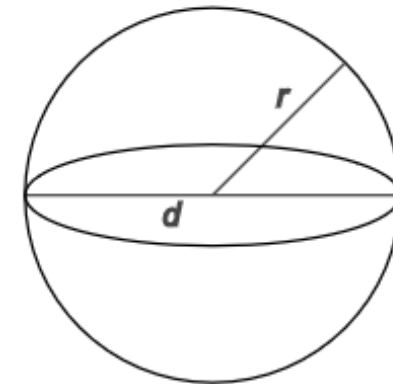
GTV=14.3cc
 CTV=88.6cc
 PTV=121.9cc

PBI CASE WITH AND WITHOUT DEVICE

SIMPLE MATH

- If you have a cavity that is **2 cm** in diameter and add a 1 cm margin for CTV, and 1 cm PTV= 4 cm diameter thus the cavity volume $4/3(\pi)r.r.r=$ 33.4cc
- If you have a cavity that is **3 cm** in diameter and add a 1 cm margin for CTV, and 1 cm PTV= 5 cm diameter thus the cavity volume $4/3(\pi)r.r.r=$ 65.25
- If you have a cavity that is **4 cm** in diameter and add a 1 cm margin for CTV, and 1 cm PTV= 6 cm diameter thus the cavity volume $4/3(\pi)r.r.r=$ 113 cc
- If you have a cavity that is **5 cm** in diameter and add a 1 cm margin for CTV, and 1 cm PTV= 7 cm diameter thus the cavity volume $4/3(\pi)r.r.r=$ 179.05

$$V = 4\pi \frac{r^3}{3}$$



FUTURE DIRECTIONS

- Currently have an ongoing pre-operative single fraction radiation Phase I trial at UTSW treating to ablative doses using SPBI techniques