Personalized Prostate Cancer Care: Focal therapy, Multidisciplinary Clinic and Prostate Cancer Clinical trials

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Disclosures

- None

Introduction

- 180,000 new cases of Prostate cancer every year
- Very varied presentation
- Varied degree of aggressiveness
- Different levels of sexual function and urination issues
- Different expectations
- One size fits all

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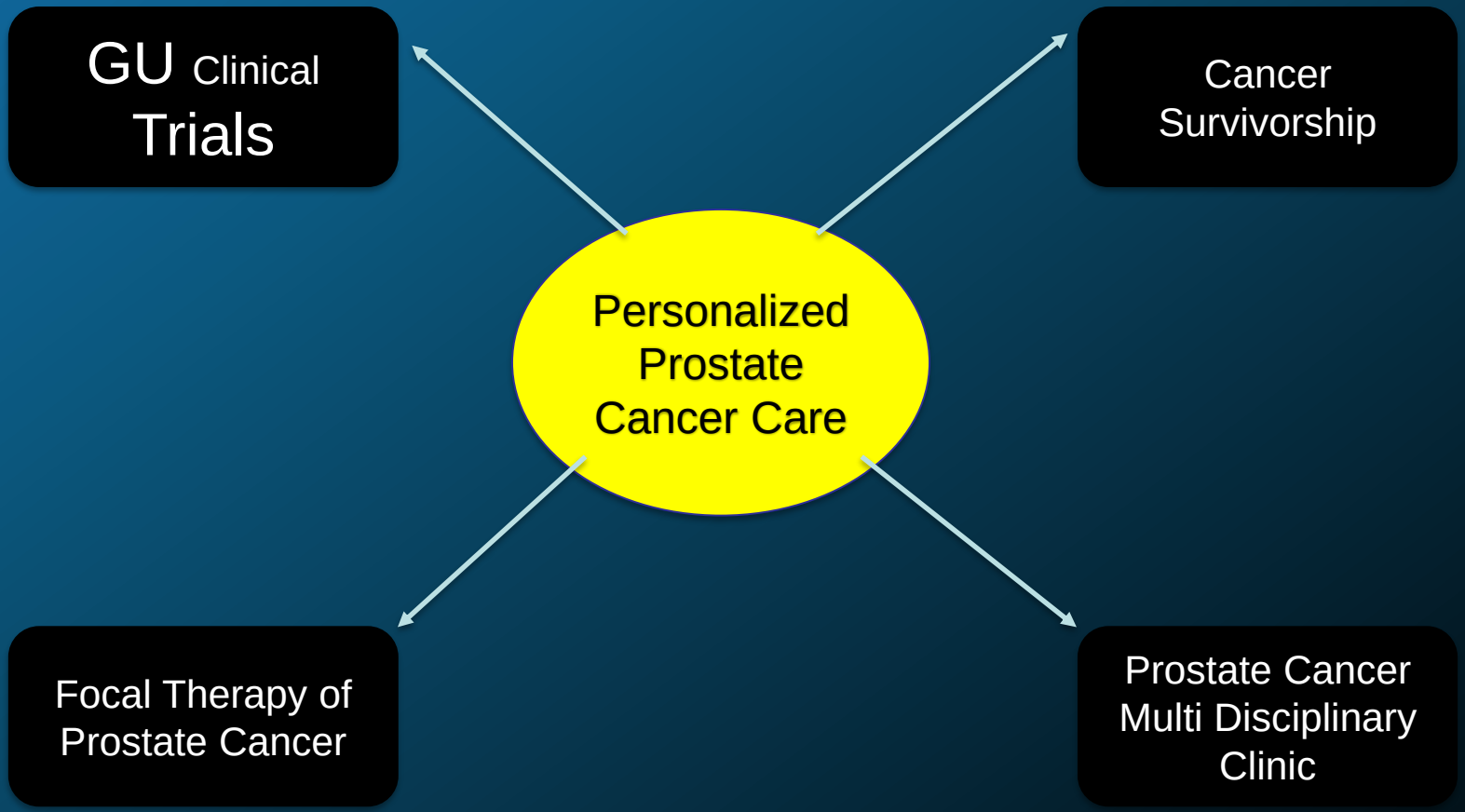

GU Clinical Trials
Cancer Survivorship
Personalized Prostate Cancer Care
Focal Therapy of Prostate Cancer
Prostate Cancer Multi Disciplinary Clinic

Prostate Cancer Multidisciplinary Clinic

- First such clinic in Greater Cincinnati Area
- Providers
  - Urologic Oncologist- Abhinav Sidana
  - Radiation Oncologist- Timothy Struve
  - Medical Oncologist- Shuchi Gulati
  - GU Radiologist- Sadhna Verma
  - GU Pathologist- Shobha Parajuli
  - Urology Advanced Nurse practitioner- Kathy Dalton
  - Cancer survivorship nurse- Beth Connor

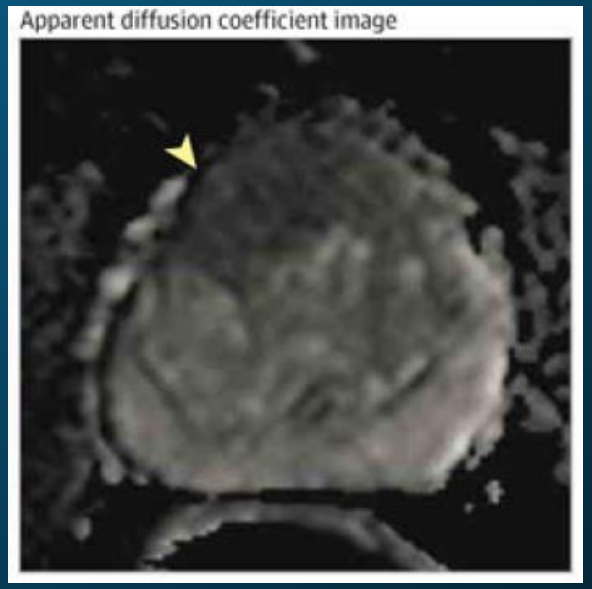
Advantages

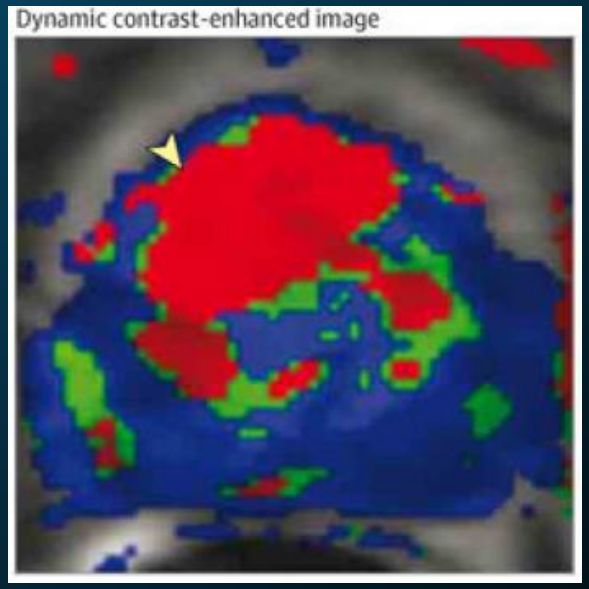
- Unbiased information
- Ability to get opinions from multiple providers at the same time
- Complex prostate cancer scenarios
- Integration into cancer survivorship, pelvic floor PT
- Offer newer treatments
- Facilitate research and teaching

Focal therapy for prostate cancer

- Focal therapy:
  - treatment that aims to eradicate known cancer within the prostate and at the same time preserve uninvolved prostatic tissue with the aim of preserving genitourinary function.
- Male “lumpectomy” that adequately treats disease and maintains QoL.
- Hypothesis: tissue preservation = functional preservation.

Multiparametric Magnetic Resonance Imaging





Targeted Bx: Cognitive fusion, in-bore and Ultrasound fusion

Siddiqui et al. JAMA 2015; 313: 390

Medium-term oncological outcomes in a large cohort of men treated with either focal or hemi-ablation using high-intensity focused ultrasonography for primary localized prostate cancer

Armando Stabile*†‡, Clement Orczyk*‡, Feargus Hosking-Jervis‡, Francesco Giganti‡§, Manit Arya*‡, Richard G. Hindley*, Louise Dickinson§, Clare Allen§, Shonit Punwani§, Charles Jameson¶, Alex Freeman¶, Neil McCartan‡, Francesco Montorsi†, Alberto Briganti†, Hashim U. Ahmed*‡†, Mark Emberton*‡ and Caroline M. Moore*‡

- 1032 patients - focal HIFU (71%) or hemiablation (29%)
- Selected based on MRI and biopsy (transrectal or transperineal)- 80% Gleason 7 or higher
- Median follow up 36 mon
- 24.7% had Gleason 7 or higher on follow up bx
- 26.3% needed retreatment, 6.6% radical treatment
- Freedom for biopsy failure: 84%, 64% and 54%, at 2, 5 and 8 years.
- Freedom from radical treatment: 98%, 91% and 81% at 2, 5 and 8 years.

MRI-US fusion guided focal/partial gland treatment at UCMC

- Motivated patient
- Understands the need for intense follow up
- Eligibility criteria:

  -MRI fusion biopsy demonstrating Gleason 7 (3+4, 4+3) in the MR visible lesion

  -Absence of Gleason 7 or high volume Gleason 6 outside of planned treatment area

  - PSA <20 ng/ml

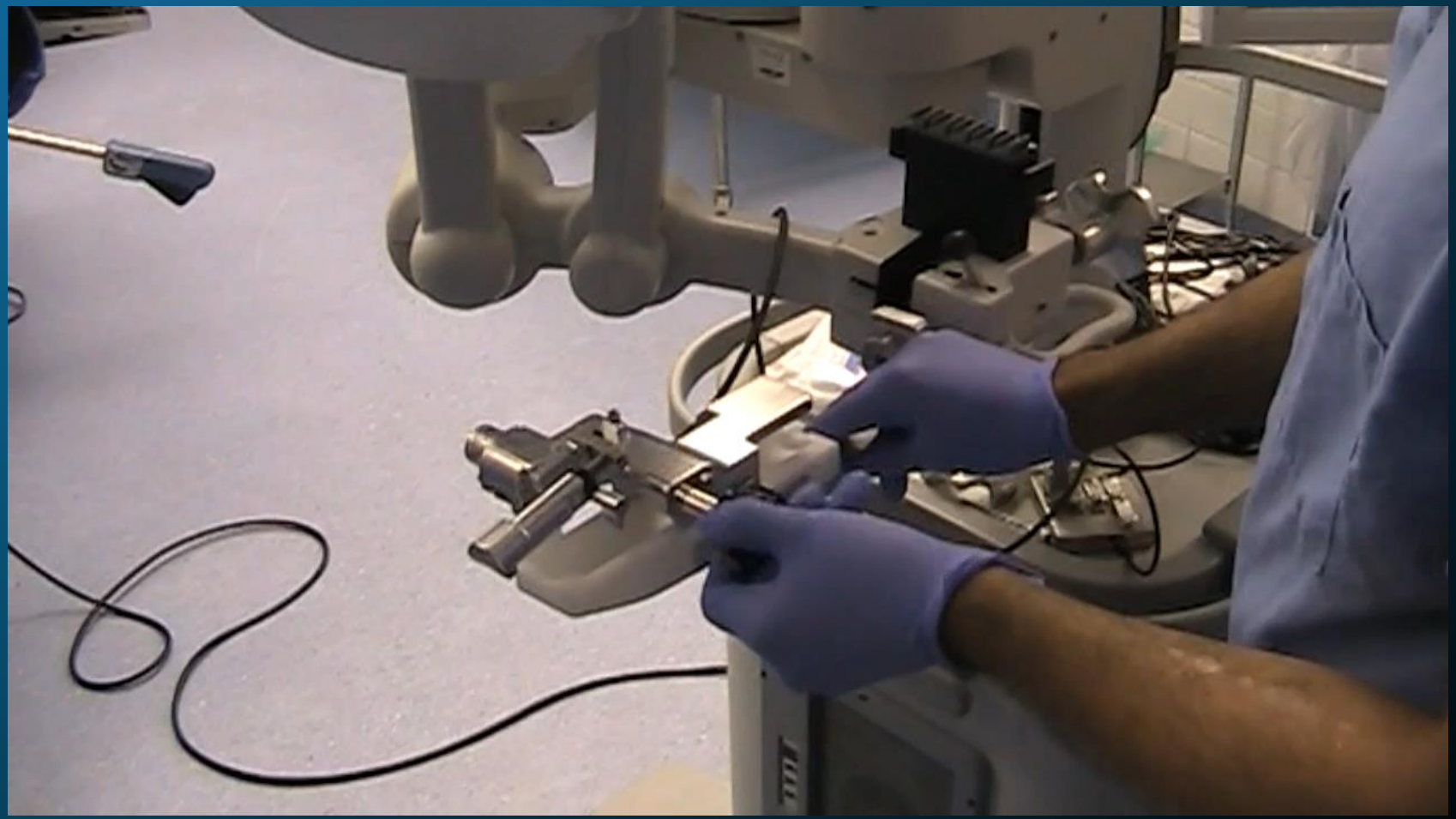
  -Treatment would spare atleast one neurovascular bundle and avoid injury to urethra and sphincter

- Cryoablation and HIFU

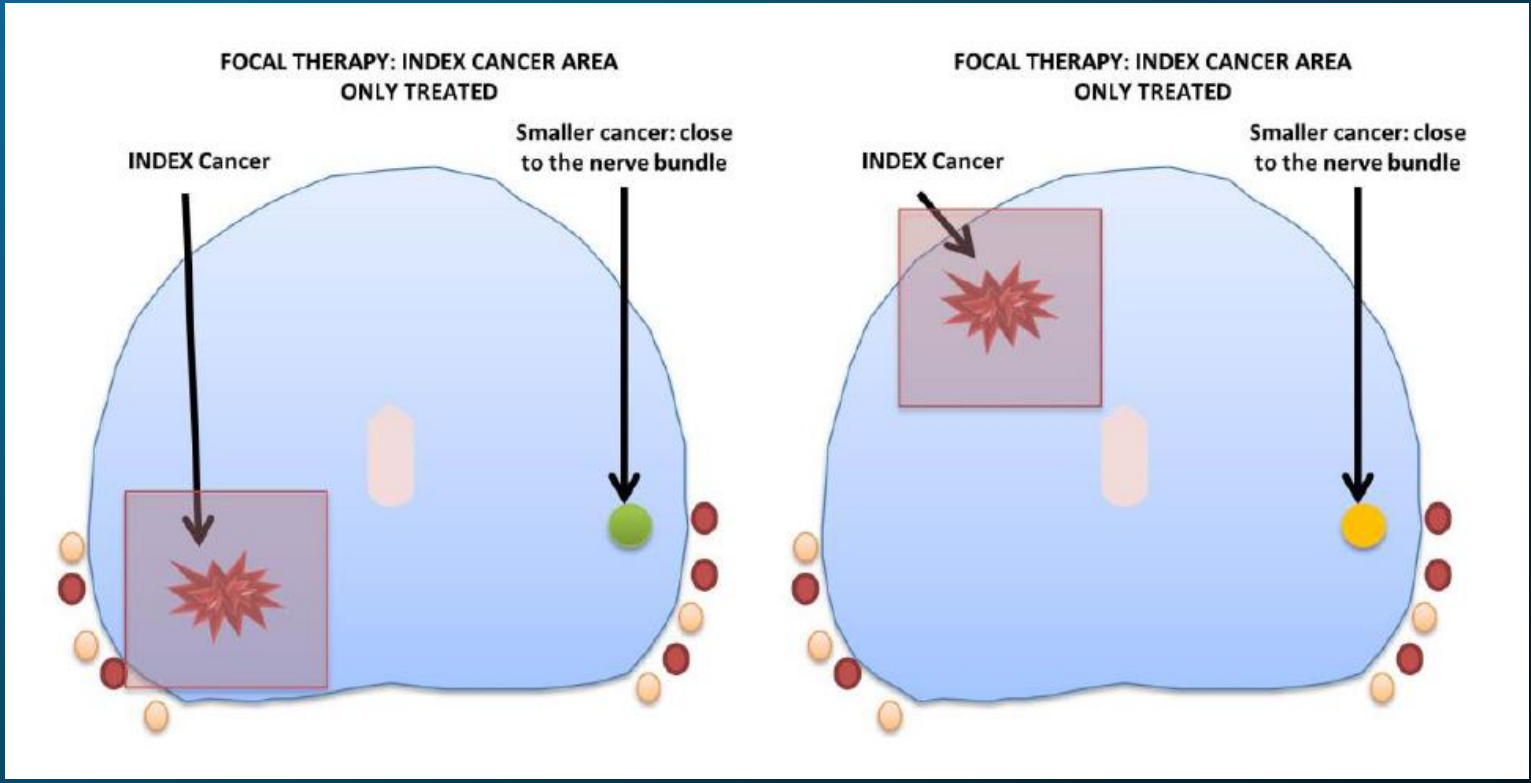
Focal therapy options for primary prostate cancer management

	Technique	Ablation	Image guidance	Number of studies (patients)	FU range	Oncological outcome	Incontinence	Urinary retention	ED
1	Cryotherapy	Freeze–thaw cycles	TRUS, mpMRI	12 (n = 2118)	6–58 mo	4–25% biopsy positive	<1%	5% (6 mo)	0–31%
2	HIFU	Heat	TRUS, mpMRI	5 (n = 171)	6–24 mo	0–21% biopsy positive	<1%	<5%	0–25%
3	IRE	Electroporation	mpMRI	5 (n = 157)	6–12 mo	3–33% biopsy positive	<1%	<3%	5–10%
4	Laser	Heat	mpMRI	6 (n = 85)	3 wk–12 mo	4–64% biopsy positive	<1%	<1%	<5%
5	Photodynamic therapy	Vascular targeting	TRUS	3 (n = 313)	6–24 mo	26–51% biopsy positive	<5%	7%	<2%
6	Brachytherapy	Radiation	TRUS, MRI dosimetry	7 (n = 541)	24–60 mo	0–17% biopsy positive	<5%	NR	NR

ED = erectile dysfunction, as defined and reported by the studies; FU = follow-up; HIFU = high-intensity focused ultrasound; IRE = irreversible electroporation; mpMRI = multiparametric magnetic resonance imaging; MRI = magnetic resonance imaging; NR = not reported; TRUS = transrectal ultrasound.

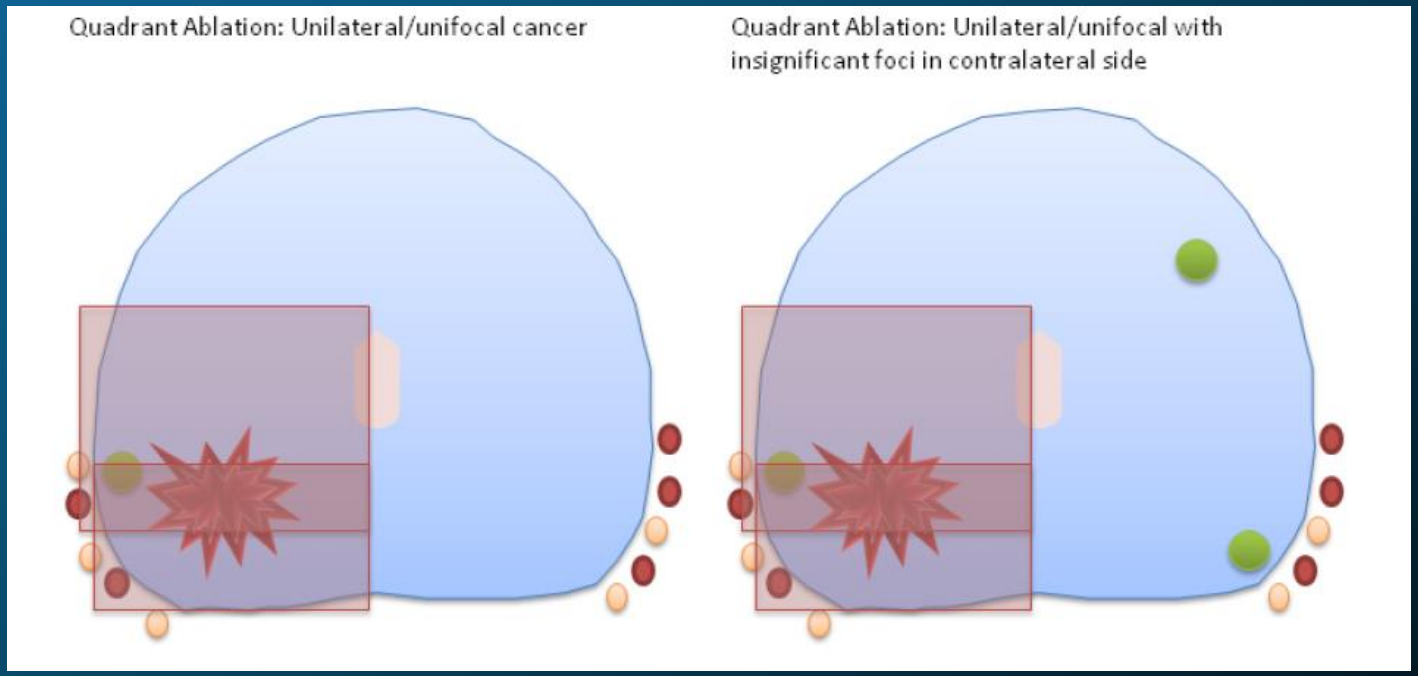


Pure focal ablation



Ahmed et al. Eur Urol 2015.68:927

Partial gland (or template) ablation



Ahmed et al. Eur Urol 2015.68:927

MRI-US fusion for focal therapy
Initial experience at UCMC

Patient Procedure Date	Age	Preoperative PSA (ng/dl)	Preop Bx Combined Gleason Score	Preoperative SHIM Score	Preoperative AUASS Score
1/16/18	71	12.3	3 + 4	18	7
2/28/18	67	4	4 + 3	10	10
6/19/18	66	6.0	3 + 4	22	8
7/16/18	76	6.6	4 + 3	24	2
7/16/18	59	9.4	3 + 4	25	9
9/11/18	64	4.6	4 + 3	5	17
9/11/18	59	6.7	3 + 4	20	1
1/29/19	60	17.8	3 + 4	25	10
1/29/19	57	0.9	3 + 4	17	1
2/5/19	56	2.3	3 + 4	6	6
4/2/19	60	5.1	3 + 4	25	2

Clinical and functional outcomes

Median Preoperative PSA in ng/dl (IQR)	5.98 (4-9.4)
Median PSA at 3 months postoperatively	2.9 (0.88-4.1)
Percent change in PSA at 3 months	-60.2 (-77.6 - -48.9)
Median PSA at 6 months postoperatively	3.2 (1.1-4.3)
Change in PSA at 6 months (%)	-65.0 (-72.5 - -29.8)
Median Preoperative SHIM score (IQR)	20 (10-25)
Change in SHIM score at 3 months	-1 (-7 - 0)
Change in SHIM score at 6 months	-4 (-11-2.25)
Median Preoperative AUASS score (IQR)	7 (2-10)
Change in AUASS score at 3 months	-2.5 (-5.5 - 1.75)
Change in AUASS score at 6 months	1 (-4.5 - 3.75)
Absence of CS cancer at 6 months (%)	83.33

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Surveillance after Focal therapy

- No clear strategy has been defined
- Traditional markers of therapeutic success and recurrence (i.e. PSA) are less relevant
- Nadir PSA and 6-month post-treatment PSA has been found to have poor correlation with residual cancer on biopsy[1]
  - May be due to the large volume of remaining prostatic epithelia, age, BPH or other nonmalignant entities[1]
- Long-term outcomes from large cohorts are not yet available to base recommended follow-up protocols after prostate focal therapy

Role of mpMRI in Surveillance

- Affords clinicians with ability to identify prostate cancer index lesions and their subsequent targeting for confirmatory biopsy and targeted focal ablation
- Provides the advantage of comparison between the follow-up and pre-ablation treatment zone
- mpMRI has high sensitivity and specificity for clinically significant cancer and a high negative predictive value with moderate positive predictive value[2]

Efficacy of mpMRI

- Dickinson et al. found that late post-treatment mpMRI at 6 months (AUC 0.77-0.85) was superior to early mpMRI at < 3 weeks (AUC 0.75-0.76) or PSA nadir/6-month PSA at subsequent biopsy[1]

- A prospective study by Guillaumier et al., analyzed 625 patients at a 5 year follow-up post-focal HIFU and found that compared to prostate biopsy, mpMRI had a NPV >=95% for clinically significant prostate cancer[3]

- Eggener el al. reported on 27 men undergoing MRI-guided focal laser ablation, follow-up mpMRI at 12 months found no suspicious lesions while 3 men actually had clinically significant cancer as detected by biopsy[4]

Current Recommendations

- mpMRI is recommended at 3-6 months, 12-24 months and at 5 years after focal therapy[7]
- Optimal frequency of imaging is not known, and periodic imaging should be determined by patient factors and resource availability[7]
- A negative mpMRI suggests a low risk of disease recurrence or progression[7]
- A positive mpMRI should lead to a targeted biopsy for histologic confirmation[7]

Conclusions

- Data on long-term surveillance outcomes for patients post-focal therapy are limited
- Multiparametric MRI (mpMRI) seems to be the most universally used and accepted imaging modality
- New imaging modalities, such as Contrast-enhanced ultrasonography, necessitate further studies to determine future efficacy in post-focal therapy surveillance in prostate cancer

S1802

- Phase III Randomized Trial of Standard Systemic Therapy (SST) Versus Standard Systemic Therapy Plus Definitive Treatment (Surgery or Radiation) of the Primary Tumor in Metastatic Prostate Cancer)

- Primary Objective:
- To compare overall survival in metastatic prostate cancer patients who are randomized to standard systemic therapy (SST) plus definitive treatment of the primary tumor versus standard systemic therapy alone.

- <u>UCCI Enrollment</u>
- 19 patients pre-screened
- 2 patients enrolled

<u>Total Enrollment</u>

Goal: 107/1273

S1802

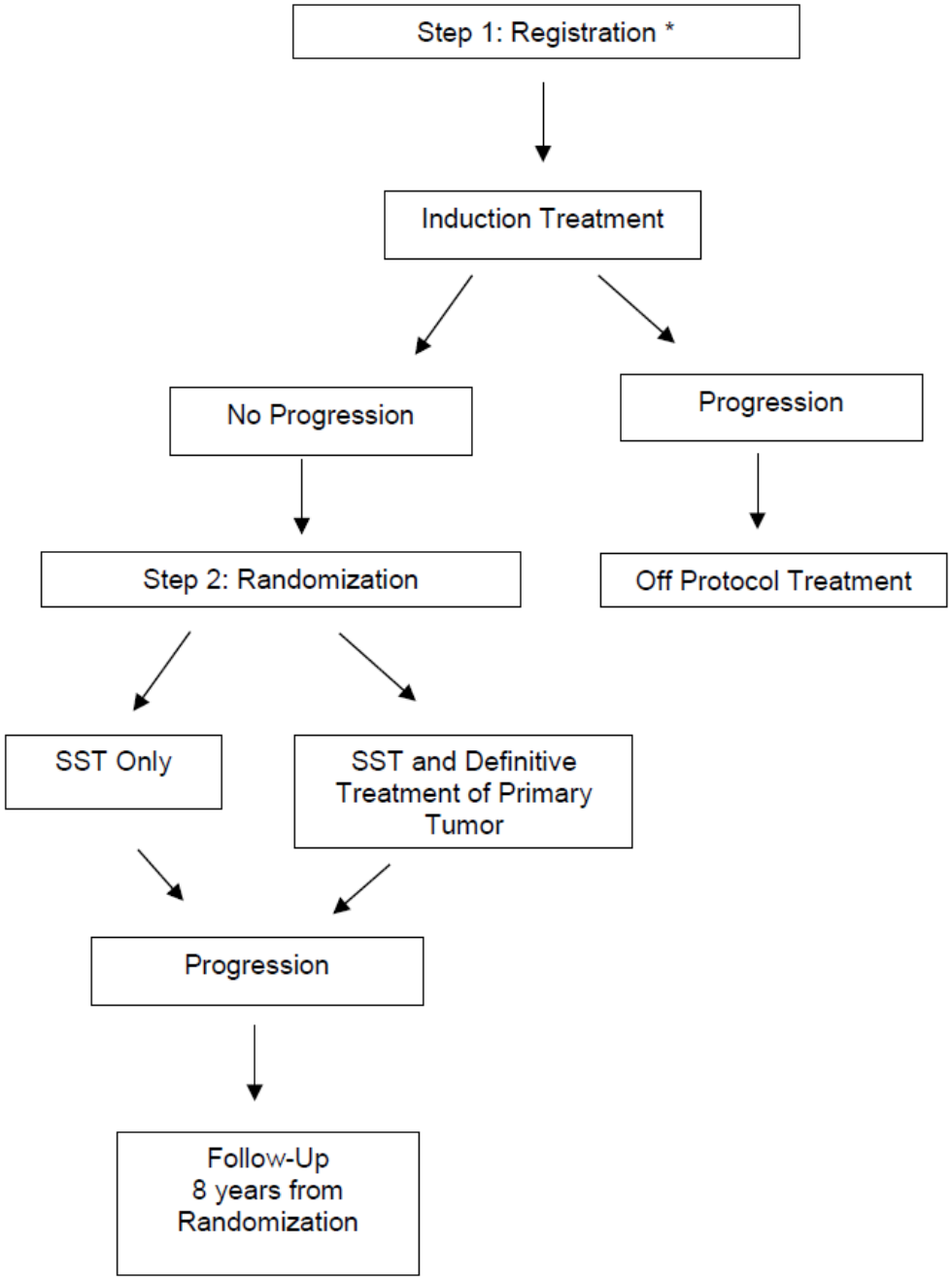
Key Eligibility

- All patients must have a histologically or cytologically proven diagnosis of adenocarcinoma of the prostate. Patients with pure small cell carcinoma* (SCC), sarcomatoid, or squamous cell carcinoma are not eligible.
- Patients must have an intact prostate. No prior local therapy for prostate adenocarcinoma is allowed (e.g., brachytherapy, HIFU, cryotherapy, laser ablative therapies). Any prior therapy for benign conditions, such as obstruction, are acceptable (e.g., transurethral resection of the prostate, greenlight laser ablation, microwave ablation).

Exclusionary Criteria:

- Patients must have received no more than 28 weeks of SST. Patients must not have progressed while on SST
- Patients must have no evidence of disease progression during the 28 weeks of SST by PSA measure, imaging or symptomatic deterioration within 28 days prior to randomization.

SCHEMA


Step 1: Registration *
Induction Treatment
No Progression
Progression
Step 2: Randomization
Off Protocol Treatment
SST Only
SST and Definitive Treatment of Primary Tumor
Progression
Follow-Up 8 years from Randomization

EOVIST

- Gadoxetate Sodium Enhanced Magnetic Resonance Imaging (MRI) as a Biomarker for Aggressive Prostate Cancer

- Primary Objective:
- To determine if Gadoxetate Sodium has the same ability as gadolinium (current standard of care contrast) to identify prostate cancer by comparing enhancement ratios.

- <u>UCCI Enrollment</u>
- 52 patients pre-screened
- 1 patients enrolled

<u>Total Enrollment</u>

Goal: 0 / 50

EOVIST

- Key Eligibility:

- Subjects with clinically localized OR advanced prostate cancer with biopsy confirmation and sufficient tissue available (obtained before Gadoxetate Sodium injection) for OATP1B3 expression.
- Subjects must have a prior MRI with gadolinium obtained as part of their standard of care for comparison available. This may have been obtained as part of an image guided biopsy.
- Serum creatinine within 3 weeks prior to Gadoxetate Sodium MRI less than or equal to 1.8mg/dl and estimated glomerular filtration rate (eGFR) must be greater than 60 ml/min/1.73m.
- Patients must have normal liver function as defined below: total bilirubin less than 2 times normal institutional limits or greater than 3.0 mg/dl in patients with Gilbert s syndrome AST(SGOT) and ALT(SGPT) less than or equal to 3 times institutional upper limit of normal

NRG GU006

- A Phase II, Double-Blinded, Placebo-Controlled Randomized Trial of Salvage Radiotherapy with or Without Enhanced Anti-Androgen Therapy with Apalutamide in Recurrent Prostate Cancer

- Primary Objective:
- To determine whether, in men with post-prostatectomy PSA recurrences, salvage radiation (SRT) with enhanced anti-androgen therapy with apalutamide will improve biochemical progression-free survival (bPFS) compared to SRT alone. A bPFS event is defined as a rise in PSA > 0.2 ng/mL from nadir, confirmed by a second PSA measurement ; clinical or radiographic local, regional, or distant metastases; or death from any cause, whichever occurs first.

- <u>UCCI Enrollment</u>
- Pre-screened: 14
- Screened: 2
- Enrolled: 2

<u>Total Enrollment</u>
Intervention: 168/324

NRG GU006

Key Eligibility

- Post-prostatectomy patients with a detectable serum PSA (≥0.1, but ≤1.0 ng/mL) at study entry (within 90 days of Step 1 registration) and at least one of the following:
    - Gleason score 7-10 (ISUP grade group 2 to 5)*
    - ≥T3a disease
    - Persistent elevation of PSA after prostatectomy measured within 90 days after surgery (PSA never became undetectable) of >0.04 but <0.2 ng/mL (PSA nadir)
- Surgical FFPE specimen must be available for submission to GenomeDx for genomic analysis on Decipher GRID platform. Results must be submitted to GenomeDx for validation and for GenomeDx to provide the subtyping needed for stratification.
- Prior androgen deprivation therapy (LHRH agonist and/or non-steroidal anti-androgen) is allowed if discontinued at least 90 days prior to Step 1 registration and given for ≤ 90 days duration.

Exclusionary Criteria:

- Prior systemic chemotherapy for the study cancer; note that prior chemotherapy for a different cancer is allowable;
- Prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields;
- Prior whole gland ablative therapy [i.e. cryoablation or high intensity focused ultrasound (HIFU)] for prostate cancer is not allowed

Thank you