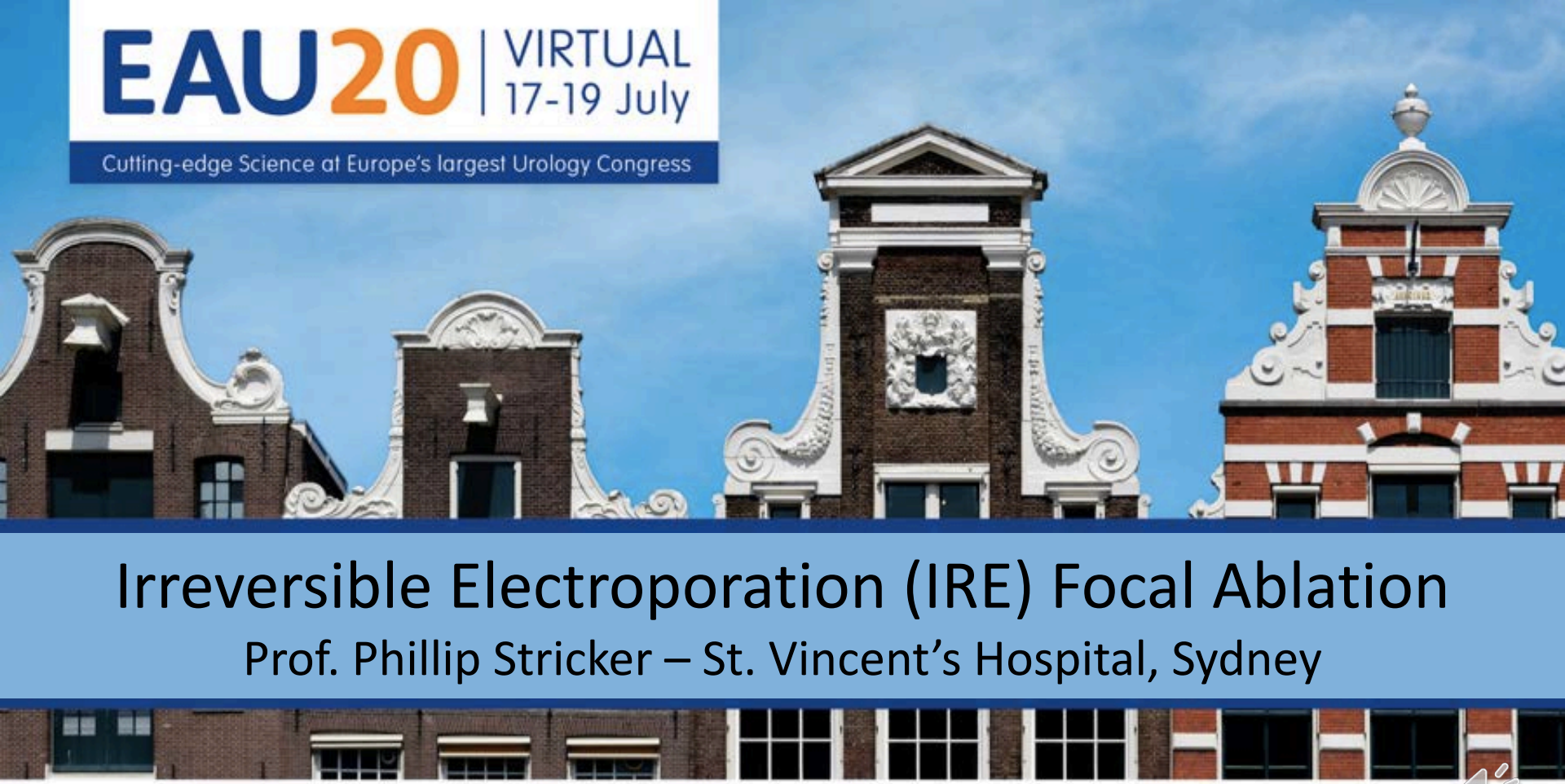


Irreversible Electroporation (IRE) Focal Ablation

Prof. Phillip Stricker – St. Vincent's Hospital, Sydney

Conflict of Interest Disclosure

I have the following potential conflict(s) of interest to report:

Consultant to Angiodynamics

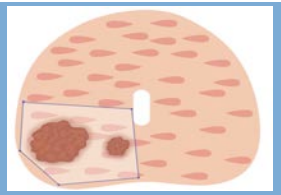
INCLUSION CRITERIA

- **Primary treatment -** Generally treat unilateral GG2; favorable GG3; majority of GG1 treated with active surveillance in our institution
- **Salvage Treatment -** Treat unilateral/focal recurrence - any Gleason score
- **Unilateral tumor -** Only treat unilateral csPCa; contralateral small foci of GG1 acceptable for treatment of index lesion
- **mpMRI -** Predominantly only treat mpMRI visible disease; otherwise quadrant or hemiablation
- **Definition of clin sign cancer –** ≥GG2
- **Location(s) -** Can treat any segment of the prostate
- **Distance tumor to apex -** place electrodes 3 mm from the apex

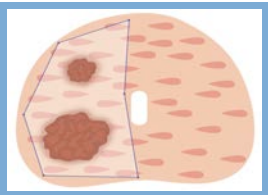
TREATMENT METHODS

- **Energy**: Irreversible Electroporation – Non-thermal ablation delivering high-voltage electric current between transperineal electrodes
- **Template**: Quadrant or Hemiablation - ”region-ectomy” not “lesion-ectomy”
- **10 mm** added to the edge of mpMRI-visible lesion
- **Catheter** placed prior to treatment - removed between day 2 and 4 – depending on pre-treatment LUTS

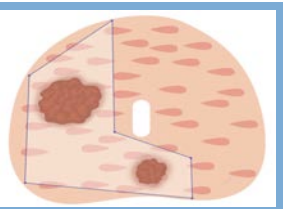
Quadrant Ablation – Index lesion with smaller significant lesion in the same quadrant



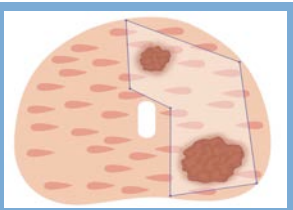
Hemiablation – Index lesion with small ipsilateral significant lesion



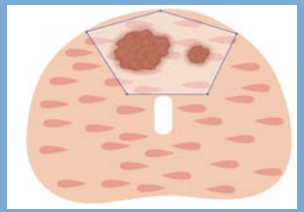
Wide Local Ablation – Index lesion with smaller significant posterior lesion



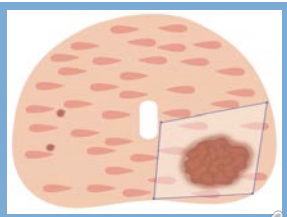
Wide Local Ablation – Index lesion with smaller significant anterior lesion



Anterior Ablation – Index lesion with smaller significant lesion both anterior



Wide Local Ablation – Index lesion with contralateral insignificant lesion



MONITORING

- **PSA** – every 3 months for the first year
- **mpMRI** – after 6 months
- **Per-protocol at 1 year :**
  - Systematic transperineal biopsy + targeted biopsy (4-6 cores)

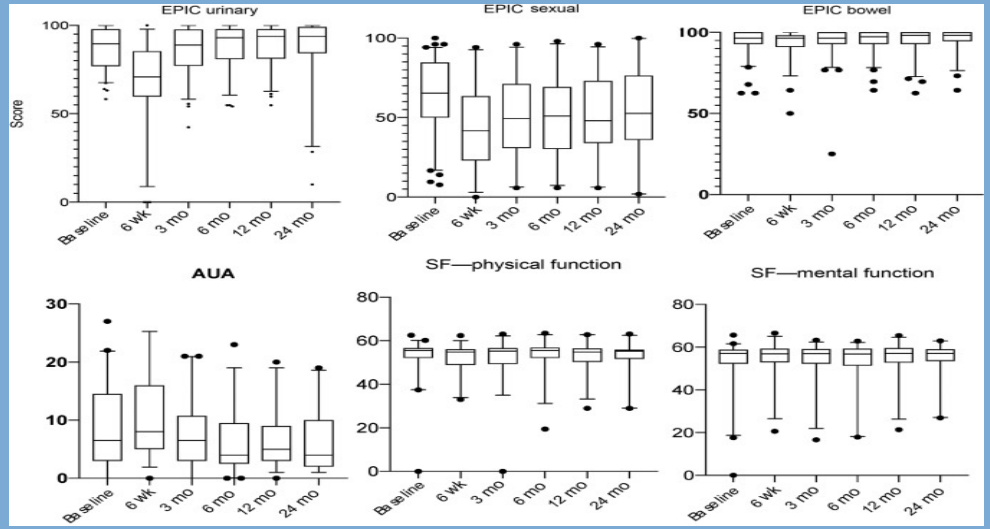
PATIENTS CHARACTERISTICS

210 patients included (primary treatment)

Age median (IQR)	**68 (61 – 73)**
Baseline PSA median (IQR)	5.9 (4 – 8.2)
Grade Group 1 n (%) Grade Group 2 n (%) Grade Group ≥ 3 n (%)	18 (8.5%) 160 (76%) 32 (15.5%)
Clinically significant cancer n (%)	91.5%
Prostate volume (cc) median (IQR)	40 (30-60) cc
Visible tumor at MRI n (%)	203 (97%)
Location Posterolateral PZ n (%) Location Apex n (%) Location Anterolateral PZ-TZ n (%)	85 (40%) 65 (31%) 60 (29%)
Median cores taken (IQR) Median positive cores (IQR)	24 (21-34) 4 (2- 6)
Follow-up median (IQR)	44 months

TREATMENT COMPLICATIONS

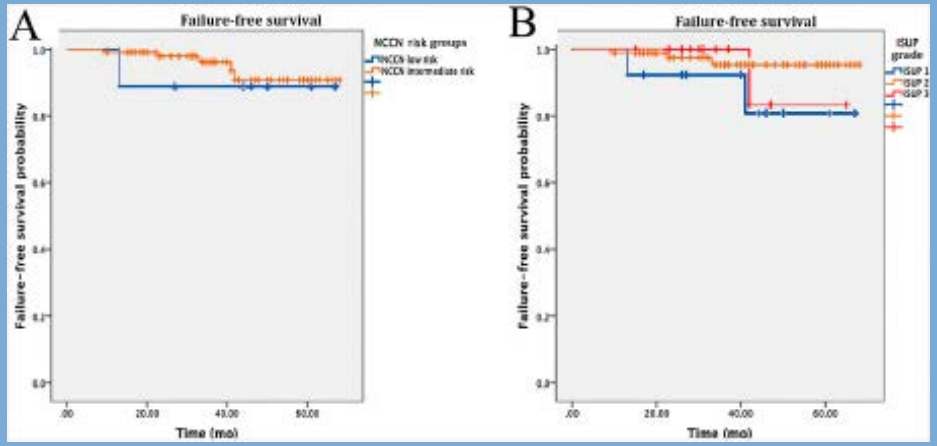
Clavien-Dindo Classification	Complication	Incidence, n/N (%)
I	Perineal pain, haematuria, dysuria, urgency, frequency,	48/210 (23%)
II	Urinary tract infection, incontinence, acute urinary retention	19/210 (9%)
III	Nil	Nil
IV	Nil	Nil
V	Nil	Nil



- 93% retained potency
- 98.8% pad free at 12 months

ONCOLOGICAL OUTCOMES

PSA Nadir	3.3 (1.2 – 5.4)
Median (IQR) cores taken Median (IQR) positive cores	25 (22-31) 1 (0-3)
In-field residual disease, n (%) Out-field recurrent/residual disease, n (%)	13 (6%) 29 (14%)



Failure-free survival – defined as progression to whole-gland or systemic treatment, or metastasis/death.

24 patients – re-do IRE ablation

Failure-free survival at 3 years 96.75%

RFS : recurrence free survival

ONCOLOGICAL OUTCOMES

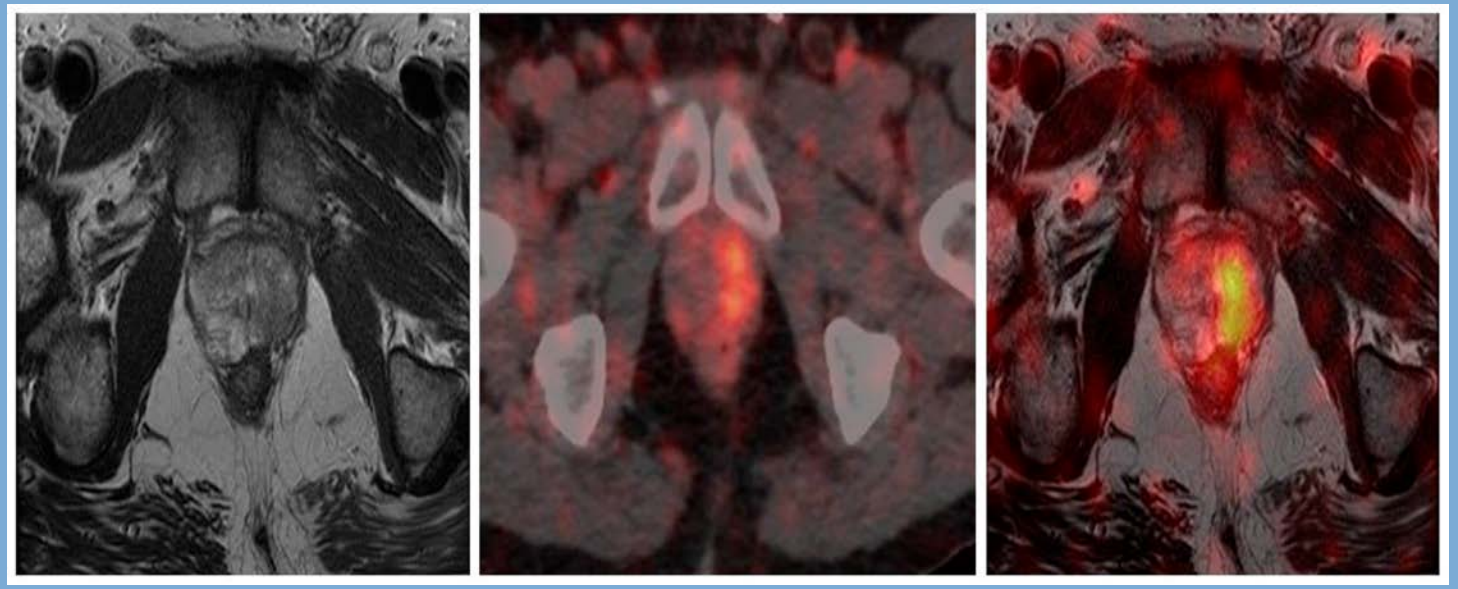
Salvage RARP post IRE ablation

- n = 16

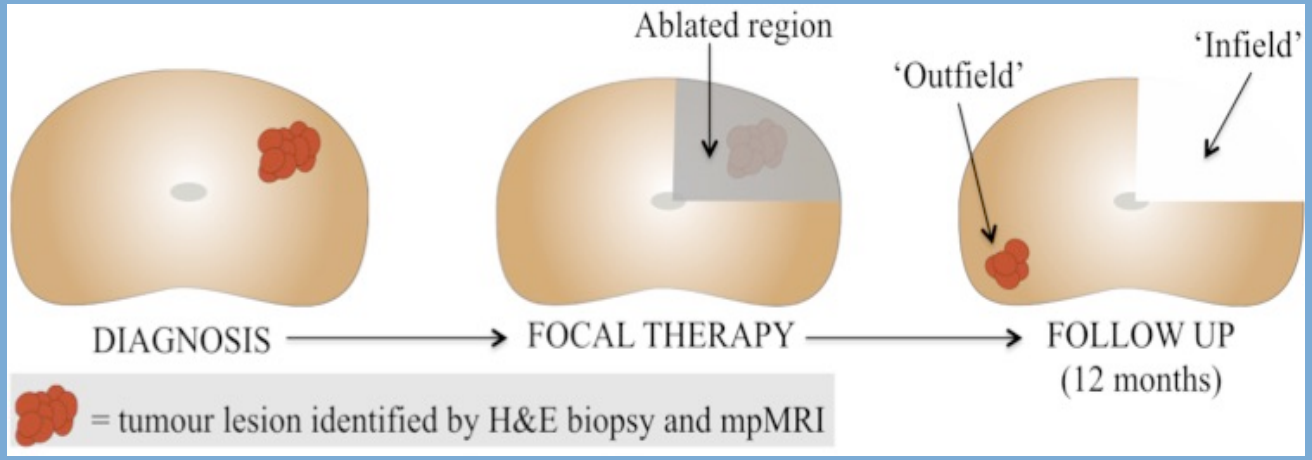
Nil biochemical recurrence (however only limited follow up at this stage).

Age (median)	66 years
PSA pre-RARP	6.1 [1.6 – 8.1]
In-field residual disease, n (%)	2 (12.5%)
Gleason grade group • 3 + 4 = 7 (GG 2) • 4 + 3 = 7 (GG 3) • 4 + 4 = 8 (GG 4) • 4 + 5 = 9 (GG 5)	 6 (37.5%) 4 (25%) 2 (12.5%) 4 (25%)
Positive Margin, n (%)	1 (6.25%)
pT2 pT3a	9 (66%) 7 (44%)
Follow up (median)	14 mo [6-30]

PSMA Pet/CT &Fusion MRI - ? The Future



Epigenetic Prediction of Failure



CIA-Pidsley/CIB-Clark/AIKorbie,
bioinformatician AI-Luu, PCa biologists AI-Risbridger/AI-Lawrence, CIC-Stricker and AIs Scheltema/Chang and pathologist AI-Delprado

IRE immune response

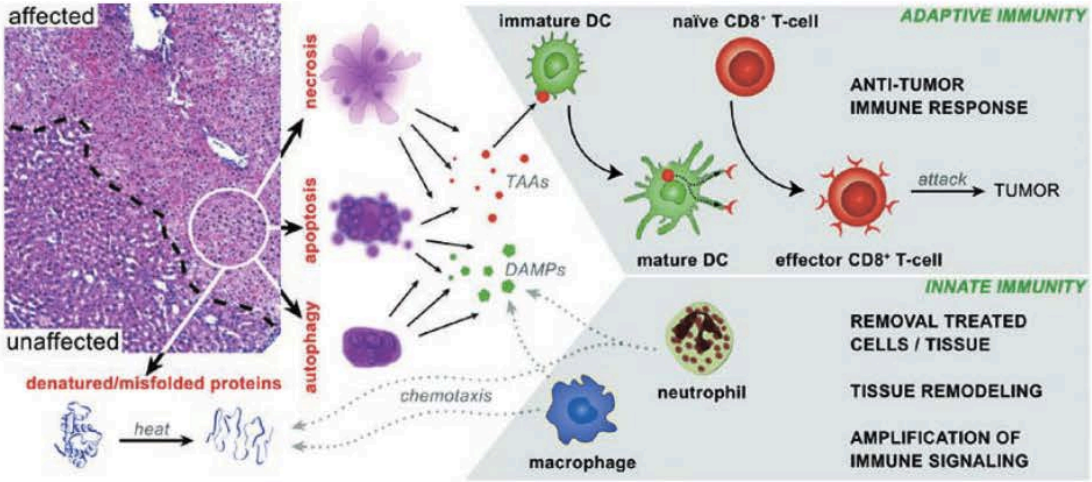


Fig. 2. Mechanistic explanation of the proposed IRE-mediated immune response. The histological section displays liver tissue in native state ("unaffected") and a tissue segment affected by IRE ("affected") (adapted from IEEE Trans Biomed Eng 2006;53(7):1409-1415), separated by the dashed line. IRE-mediated Joule heating as well as electrical effects cause protein denaturation and the induction of various forms of cell death (necrotic, apoptotic/necroptotic, autophagic), which leads to the release of damage-associated molecular patterns (DAMPs) and tumor-associated antigens (TAAs). The DAMPs facilitate chemotaxis of neutrophils and macrophages to the treated region, which leads to the effects specified under "INNATE IMMUNITY". The TAAs are processed by cells of the adaptive immune system that subsequently mount an anti-tumor immune response to eliminate the tumor cells, which may include abscopal effects.

Heger et al. Hepatobiliary Pancreat Dis Int, Vol 14, No 3 • June 15, 2015