Introducing IRE

IRE Symposium
The Harvard Club
January 22, 2009
The presentations made at the January 22, 2009 IRE Symposium represent the personal experience and opinions of the individual physician-investigators. The uses and results reported herein reflect the use of the device as part of the practice of medicine by these physicians and do not constitute a recommendation or representation by AngioDynamics that such uses are safe or effective. The NanoKnife IRE system is FDA cleared for use in the United States for the ablation of soft tissue and AngioDynamics does not promote, market or recommend the NanoKnife for any specific clinical indication. The information in this document is provided on behalf of, and for the convenience of, the physician-investigators who presented at the seminar and may not be divulged, disseminated, provided to a third party or reproduced without their written consent.

The NanoKnife IRE System carries the following statement as an integral part of its labeling: CAUTION Federal or US Law Restricts the Use of the Device by or on the Order of a Physician.
The Use of Nanoknife System To Treat Focal Prostate Cancer in Low Risk Patients: A Pilot Safety Study

Maurizio A. Brausi
Professor and Chairman of Urology
Ausl Modena, Italy
Focal Therapy In Pca: Concept

- Pca is the most common cancer among men in the US and is second only to lung cancer as cause of cancer death.
- In 2007, 27,050 Americans will die of Pca and 218,890 new cases will be diagnosed.
- The advent of PSA test and screening programs lead to early diagnosis which comprises also small foci of isolated or multiple cancer.
The current standard primary treatment of localized PCa is radical prostatectomy or radiation therapy. However, studies of men in post RP recovery show that 44% to 75% experience sexual dysfunction and up to 20% incontinence (Mattew J. Urol 2005). External radiotherapy is associated with rectal morbidity and bowel symptoms and ED in time (Bhatnagar et al Pca Prostatic Dis 2006).
Focal Therapy In PCa

- New treatment modalities that can maintain the excellent treatment outcomes of RP while diminishing the morbidity have been searched.
- Focal, minimvasive therapy (Cryotherapy, Brachytherapy, HI-FU) goals: to eradicate local cancer with equal efficacy but with few or no side effects.
- Electroporation can certainly be included in this group of minimvasive focal treatments.
Focal Therapy: Advantages

- Curative and survival rates comparable with those of conventional surgical and radiation therapy
- Simple techniques
- Short hospital stay (1 day) or day surgery
- Faster recovery
- Fewer complications (DE, incontinence, rectal injury)
Focal Therapy: Drawbacks

- Risk of incomplete treatment (missed cancer foci)
- Inadequate ablation to target tissue
- Not applicable to all patients (Not indicated when periurethral or extraprostatic extension)
- Difficulty in monitoring efficacy and recurrence for lack of PSA guidelines
- No final path. report (Gleason Score, margin status)
Multifocality is a theoretical contraindication to focal ablation.

No accurate data on unifocal Pca available. Djavan B, Tech Urol :1999, reported 33.1% unifocality in RPs. Moreover…….

About 80% of tumours are of small volume (<0.5ml) and are insignificant.
How Can We Select Pts. For Focal Therapy?

- Sextant TR US-guided biopsy is not accurate: it cannot predict unilateral disease
- Increased number of prostatic biopsy (extended) is needed
- Computerized 3-dimensional real time topographic reconstruction of the prostate has been developed to facilitate the identification of clinical significant cancers (>1ml).
- Grid to increased N of cores (50-112) according to prostate volume (Onik, Brausi 2008) is another option
Electroporation (NanoKnife)

- When we apply an electric current to a cell the membrane pores open. This phenomenon is reversible if we administer it for a short period of time. If we persist we reach the irreversible point and cause cell necrosis.
- This is the concept of nanoknife device
- We produce tissue necrosis in a given area of the prostate through a needle inserted under US
DEVICE (NANOKNIFE)

ELECTRODE PROBE

Device Length 15 cm
Active Length 0-4 cm
Objectives

Primary: to test the procedural and short term safety of the Low Energy NanoKnife System when used to ablate Pca

Secondary: to evaluate the short term effectiveness of the device
Inclusion Criteria

- Age 65-80 years
- Histologically confirmed T1c-T2 Pca
- Gleason score <6
- Psa < 10 ng/ml
- No significant median lobe (<2cm) on US
- Good visualisation of prostate gland on US
- No prostate calcification > 5mm
- Ability to stop anti-coagulant therapy for 7 days prior and 7 days post procedure
Exclusion Criteria

- Active UTI
- History of bladder neck contracture
- ASA IV or greater
- Interest in future fertility
- History of inflammatory bowel disease
- Concurrent major debilitating illness
- Prior or concurrent malignancy except skin cancer (no Melanoma)
Exclusion Criteria

- Prior or current therapy for Pca
- Biologic or chemotherapy for Pca
- Hormone therapy within 3 months of the procedure
- TURP, urethral stent
- Prior major rectal surgery (except hemorrhoids)
Baseline Evaluation

- History
- Physical Examination including Digital Rectal Examination (DRE)
- AUA Symptom score questionnaire (I-PSS)
- International Index Erectile Dysfunction Examination (IIEF)
- Lab Exams + Psa total/Free, Ratio
- Trans-Rectal Ultrasound (TRUS): visibility of the gland, diameters, calcifications
Prostate Biopsy Procedure

- Biopsies are performed with the use of a reproducible coordinate grid system with a stand to support the grid.
- The trans-perineal approach under anesthesia is performed. Biopsies at 5 mm interval in the transverse plane are taken.
- The number of cores according to prostate volume (1.6-1.8 biopsies per cm³) (Focal Treatment Conference Urol 2007)
Technology for Prostate Biopsy

- US machine: Esaote-Hitachi H-19
- Probe: Biplane Sound 7.5
- Grid with a Stand supporting it to ensure the reproducibility of the manoeuvre
- Needle: 22 gauge
- Gan machine (Bard)
Hitachi H 19

Accessories for procedure and transperineal biopsy

Stand
Pathology Report

- The end of each prostate core should be marked with ink.
- Path Report should include:
  - Length of the core, size and location of >1 cancer in the core
  - Location of the cancer in relation to the marked end
  - Gleason score
  - Molecular Markers (?)
Low Risk Pca : Definition

- AUA Guideline 2007
- cT1c-T2a
- Gleason Score < 6
- Psa < 10 ng/ml
Treatment

- Operating Room (cysto room)
- Patient in lithotomy position
- General anesthesia
- Patient will be sterilely prepared and draped
- A 20 F Foley catheter will be placed
- Biplane Trans-rectal US probe placed in the rectum and the prostate visualized in sagittal and axial views
Treatment II

- Prostate is divide in 4 segments
- Probe pairs will be placed starting at 12.00 position spaced 1 cm apart
- The overlapping ablations cause complete coverage of the quadrant of the gland
- For each quadrant the probes are placed according to the procedure previously described
Treatment III

- Treatment application will be focused on the known areas of cancer
- The objective is to ablate the cancer area (reasonable diameter) without needing to ablate the entire prostate if possible
- Probes are placed in the prostate transperineally with the aid of the same grid used for biopsies in order to place the probe in the same area where cancer has been found
First Clinical Procedure
Follow-UP

- Patients will be controlled at day:
  - 14 : Visit (side effects), Psa, I-PSS, IIEF
  - 30 : Visit, Prostate biopsy under US in the same area where tumor was treated (15-30 cores), Psa, I-Pss, IIEF
  - 90 : Visit, Psa, I-PSS, IIEF
  - 180:Visit, Psa, I-PSS, IIEF
Electroporation (NanoKnife) in Pca: First Results Pilot Study

- N Patients who had biopsies: 15
- Mean age: 69 (range 59-77)
- Mean Psa: 6.23ng/ml (r 3.20-.76)
- Mean N cores: 75.8 (r. 38-117)
- Prostate volume: 61.2 (r 26-80cc)
- N Pca detected: 7/12 (58%) all <1cc (3 wait)
- Complications: 2 Urinary Retentions (catheter for 1 day)
Patients Characteristics: Baseline

- 5 patients recruited for the study
- Mean Psa : 5.65 (range 3- 8.46)
- Mean I-IEF : 16.8 (range 14-22)
- Mean I-PSS : 11.8 (range 0-23)
Electroporation (NanoKnife) in Pca: First Results Pilot Study

- N patients treated: 6
- 1 had recurrent disease after cryo and radiotherapy for advanced Pca (off)
- 5 pts. had low risk Pca (c T1c, Psa<10ng/ml, Gleason <7)
- 4/5 in only one area of a prostate lobe (4-6 needles) , 1/5 in both lobes
- General anesthesia was always used
Results at 14 days

- Side effects: 1 urinary retention (Foley catheter for 1 week), 1 Urge Incontinence (transitory: 2 days)
- I-IEF (mean) : 15.2 (1.6 decrease)
- I-PSS (Mean) : 6.2 (5.6 decrease)
Results at 30 days

- Side effects: 0
- Psa (mean) : 3.4 ng/ml (2.25 ng/ml decrease)
- I-IEF (mean) : 13  (3.8 decrease base)
- I-PSS (mean) : 6.2 (5.6 decrease)
- All pts. had prostate biopsies : mean N cores = 21.2 (15-30)
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<td>C.G.</td>
<td>7.2</td>
<td>2.3</td>
<td>30</td>
<td>17</td>
<td>16</td>
<td>12</td>
<td>7</td>
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<td>5</td>
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<tr>
<td>M.E.</td>
<td>3</td>
<td>2.6</td>
<td>15</td>
<td>22</td>
<td>21</td>
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<tr>
<td>C.T.</td>
<td>5</td>
<td>1.8</td>
<td>24</td>
<td>16</td>
<td>1</td>
<td>2</td>
<td>21</td>
<td>6</td>
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<tr>
<td>B.V.</td>
<td>4.4</td>
<td>7.3</td>
<td>16</td>
<td>14</td>
<td>18</td>
<td>12</td>
<td>9</td>
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<tr>
<td>M.A.</td>
<td>8.46</td>
<td>3</td>
<td>21</td>
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<td>20</td>
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<tr>
<td>M. Value Range</td>
<td>5.65 (3-8.46)</td>
<td>3.4 (1.8-7.3)</td>
<td>21.2 (15-30)</td>
<td>16.8 (14-22)</td>
<td>15.2 (1-20)</td>
<td>13 (2-17)</td>
<td>11.8 (0-23)</td>
<td>6.2 (0-10)</td>
<td>6.2 (0-16)</td>
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</table>
**Conclusions**

- Focal Therapy (lumpectomy) is a very attractive concept and well accepted by our patients.
- A systematic, accurate early diagnosis with the use of grid allowing 1.8 biopsies/cm³ of prostate is a must.
- Electroporation using NanoKnife System is safe and simple. With the grid the Pca area diagnosed at biopsy can be easily treated.
Conclusions II

- The results at 30 days on PSA (mean reduction of 2.25 ng/ml) are very encouraging
- An improvement in patients symptoms has been observed (5.6 reduction)
- Side effects are mild
- We are waiting for the control biopsies at 30 days
Conclusions III

- This technique has a possible bright future for the treatment of Pca
- It must be studied and analyzed very carefully trying to find all the possible ways for improvement
- Personally I am very excited and I strongly believe in it!
- (Brausi MA, New York, January 2009)
Apply Treatment

- US imaging performed to confirm appropriate probe placement
- Connect the probes to the generator
- The device performs a pre-test prior the treatment to confirm the probes are not touching
- Make sure the probes are properly plugged
Treatment

- The treatment parameters (first quadrant) will be 1,000v-2,500v, 100 nans and 90 pulses for each probe pairing.
- Once the probes are in the correct position a 22 gauge spinal needle will be placed into Denonviller fascia and approximately 25cc of D5W will be injected into Denonviller fascia to separate the rectum from the prostate capsule.
- At the end of treatment remove the probes.
- Foley will be left in place for 1-2 days.
Measuring the prostate: standardized measurements of the anterior, posterior, width and length will be made on US.

Positioning the first pair of probes: starting at the midline of the prostate, position the first probe at 12.00 with the second placed 1 cm away, directly below it. If the urethra is too close, move the probe pairing off the midline.
Complications

- 1 Pz Transitory Urinary Retention (Bladder Cateter Foley for 7 days)
- 1 Pz Transitory Urge Incontinence
Irreversible Electroporation: Expanding the Role of Image-Guided Cancer Therapy

Damian E. Dupuy, M.D.
Professor of Diagnostic Imaging
Alpert Medical School of Brown University
Director of Tumor Ablation
Rhode Island Hospital
What Is Ablation?

“The removal or destruction of a body part”
Ablative Methods

Fry-freeze-pickle-electrocute

• Heat
  - Radiofrequency energy
  - Microwave
  - Laser
  - High intensity focused ultrasound (HIFU)

• Cold
  - Cryotherapy

• Chemicals
  - Ethanol
  - Acetic acid

• Electrochemical
  - Irreversible electroporation
  - Galvanometry
Benefits of Ablative RX

- Safe outpatient band-aid procedure similar to biopsy
- Controllable ablation zone
- Synergy with existing cancer therapy
- Repeatable (e.g., retreatment toxicity less in target field)
Thermal Ablation Devices
Applications

- Liver Tumors
- Lung Tumors
- Renal/adrenal tumors
- Bone Tumors

Breast tumors
Head and Neck malignancies
Pelvic recurrences

95% Clinical Volume
Ablative Therapy
Palliation

• Majority of oncology is palliation
• Ablation can provide meaningful palliation
• Synergy with conventional therapy
• No limitations of repeat therapy
Pitfalls of Thermal Ablation

- Collateral damage prevents use in central location of liver, kidney, lung
- Thermal sink effects prevent complete kill near larger vessels and airways
- Kill zones unpredictable
- Thermal injury is painful
Potential Benefits of IRE

- Treatment is not affected by vessels or airways
- Ablation zone predictable
- Underlying tissue scaffolding is not damaged like it is with some thermal ablation techniques
- Post-op pain minimal similar to biopsy
70 yo ♀ With 4cm Kidney Cancer
Poor Surgical Candidate

- Opposite kidney impaired due to prior stone extraction and lithotripsy
- Right sided heart failure-respirator dependent via tracheostomy
- Despite her medical conditions she lives at home and can participate in cooking and cleaning around the house
4cm Central RCC*
Kidney Function by Side
Treatment options

- Surgery would likely leave her dialysis dependent even if she could medically tolerate nephrectomy.
- Radiofrequency ablation or cryoablation not likely to completely destroy all viable tumor due to vessel proximity.
- IRE was felt to be best option due to anatomic location.
IRE
6 monopolar Electrodes

Immediate Post-IRE
Central necrosis and no collecting system Injury
Potential Future Opportunities

- Brain and spine tumors
- Central tumors in the chest, liver and kidney
- Pancreatic tumors
- Musculoskeletal tumors
- Nerve tumors
Irreversible Electroporation

- 2500-3000 volt DC microsecond pulses
- Puts holes in cell membranes leading to cell death in hours
- No thermal effects so may be used near airways and vessels
Irreversible Electroporation
Swine Lung

interlobular septum* separating involved lobule from adjacent intact parenchyma

reparative/fibrosing changes, with mild chronic inflammation
Irreversible Electroporation

• If airway and blood vessel damage is negligible perhaps IRE may have new applications in the treatment of NSCLC?
Irreversible Electroporation: A New Non-Thermal Ablation “Nanoknife”

Stephen T. Kee, MD
Associate Professor of Radiology
UCLA Medical Center
What is ELECTROPORATION?

1. Technique that increases the permeability of cell membranes by changing the transmembrane potential resulting in disruption of the cell membrane

Application of short pulse high-voltage DC current
History of Electroporation

- Idea first proposed in mid-1960s
- Reversible Electroporation used in
  1. Electrochemotherapy
     - Delivery of non-permeable chemicals into cells
  2. Electrogenetherapy
     - Delivery of nucleic acids and DNA into cells
- Irreversible Electroporation???
  - First used to exterminate microbial organisms
Reversible Tissue Electroporation
(http://www.inovio.com/)

Intralesional injection of the macromolecule.

Insertion of the Electrode Applicator into the tumor.

Reversible Electroporation

"I have stated in public seminars that, in my opinion, electroporation is the gold standard for DNA vaccine delivery, giving us the best result in terms of immunogenicity of DNA vaccines."

George N. Pavlakis, MD, PhD
Chief, Human Retrovirus Section, Vaccine Branch
National Cancer Institute

UCLA Interventional Radiology
David Geffen School of Medicine at UCLA
Exposing a cell to an electric field can have a number of predictable outcomes.

Figure 1. Exposure of a cell to an electric field may result either in permeabilization of cell membrane or its destruction. In this process, the electric field parameters play a major role. If these parameters are within certain range, the permeabilization is reversible; therefore, it can be used in applications such as introduction of small or large molecules into the cytoplasm, insertion of proteins into cell membrane, or cell fusion.
Irreversible Electroporation

- Rubinsky et al. suggested possible use of Irreversible Electroporation to induce cell death in cancer cells.
- Creates a focal, well-margined area of cell death with membrane disruption, vacuolar degeneration, resulting in Apoptosis in **MILLISECONDS**.
- Non-Thermal (below 50°C) Ablation
- Real-time monitoring with ultrasound

**Advantage:** real-time monitoring, short procedure time, larger ablation area, no heat-sink effect
Irreversible Electroporation

- For **reversible** use - up to 1kV, 100 μsec pulses
- To achieve irreversible use – multiple (80) short pulses, 100 μsec, but with a higher voltage, 1.5 - 3kV

- Limitation – what distance between probes??
  - It appears that an electrical field can be established as long as the generating electrodes are less than 3-4 cm apart

- Beyond this distance get local charring at the electrode, “sparking”
First generation IRE generator
Modern generator (Electroporator)

Generator (AngioDynamics)

- Energy output - 3kv pulses,
- 50 amp maximum energy output

• Default treatment parameters for 2, 3 and 4 cm treatment zones. Plus a “custom” section that allow the physician to design treatment arrays
Technique (Probe)

**Single probe x 2**
- 19 gauge needle
- Echogenic surface
- Maximum depth = 15 cm
- 1.5 cm spacing = 2 × 3 × 3 ablation zone

**Bi-polar probe**
- 16 gauge needle
- Echogenic surface
- Maximum depth = 18 cm
- Single probe = 2 × 2 × 3 ablation zone
Irreversible Electroporation

- Needle placement under Ultrasound guidance
Irreversible Electroporation

- Ultrasound monitoring immediately after the electroporation
Irreversible Electroporation (IRE)
Treatment planning examples
Irreversible Electroporation (IRE)
Treatment planning examples
Treatment planning works very well with IRE..........

Rubinsky, B., Onik G., Mikus, P. “Irreversible Electroporation: A New Ablation Modality - Clinical Implications”


UCLA Interventional Radiology
David Geffen School of Medicine at UCLA
.... but this is what will happen if you do not plan well or do not pay attention to the plan.
Irreversible Electroporation

Previous in vivo experiment demonstrated
- Using 4 probes with relatively lower voltage and pulses to create approximately 5 cm size lesion

In our current study,
- Using a single probe or 2 probes with higher voltage and more pulses 3.5-4cm lesion was created

Using a single needle (bipolar) create a 2.5-3cm lesion

Can’t just keep increasing distance between probes as there is a physical limitation where a stable electrical field can be produced

Can increase distance and increase voltage, but get peri-electrode heating/charring instead of field
US Image at Treatment
Results

- Contrast enhanced CT
Results

- Contrast enhanced MRI (GRE TE2.32/TR257 – pre/post)
Results

- US 24 hrs after the treatment
Results

Liver
Results

Liver

Vessels
Results

Kidney
Results

Pathologic Analysis (H&E)

H+E staining shows cellular destruction 24 hours after treatment
Results

- Pathologic Analysis (Von Kossa)
- Stains for intracellular calcium, definite sign of cell death
Cell death without architectural distortion (Apoptosis)
Pathology Report stated that,

**Histopathology:**

A. Liver: The ablated area consists of two oblong regions that coalesce at the deep margin of affected area. One of the affected regions is continuous from the capsule surface and the other has a separation from the capsule surface by 2-3 viable hepatic lobules. The capsular surface has multifocal necrosis that extends 2-3 lobules into the hepatic parenchyma (except in the continuous area as described above). Areas of necrosis are characterized by cellular debris, congestion and small to moderate numbers of mixed inflammatory cells consisting of neutrophils, eosinophils, macrophages and lymphocytes. Necrotic lobules have hyper eosinophilic cytoplasm and pyknotic nuclei. Multifocal aggregates of necrotic hepatocytes have intracytoplasmic basophilic granular material consistent with calcium. The ablated

- **IS IT REALLY A CELLULAR NECROSIS??**
- **More likely a form of Apoptosis, cell death with preservation of architecture**
Results

Pathologic Analysis (TUNEL)

TUNEL stain is a good indicator of Apoptotic cell death, cell death without architectural destruction.
Results

Pathologic Analysis (vonWillebrand Factor)

Stain demonstrates integrity of vessel wall in treated region

?relevance?
Results

Contrast enhanced MRI (VIBE TE1.84/TR4.59 - post)
Results

MRI - DWI
Irreversible Electroporation

Questions that have been investigated

1) Do these pulses actually kill tissue?
2) What are the optimum parameters?
3) How far apart should the electrodes be?
4) How clearly defined is the “kill zone”
5) Can anything be imaged?
6) What happens to blood vessels and bile ducts?
7) What is left behind, scar, cyst, etc.?

8) What happens to cancers?????????
How clearly defined

- Would appear that there is a very narrow “zone of transition”
- All histology to date has shown dead tissue sharply demarcated from healthy liver
Body’s reaction

- How will the body deal with this?
- The simplest explanation, although by no means proven, is that the body will deal with these cells as if they have aged and died, treating them as natural debris and phagocytosing them over a period
- If this is in fact the case then perhaps long term we will see “nothing” just regrowth of normal tissue
Results (Time Course Experiment)

Engorged local lymph nodes

<table>
<thead>
<tr>
<th>Gross</th>
<th>1 day</th>
<th>3 days</th>
<th>7 days</th>
<th>14 days</th>
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<td></td>
<td><img src="image1.png" alt="Image" /></td>
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| 40 x  | ![Image](image9.png) | ![Image](image10.png) | ![Image](image11.png) | ![Image](image12.png) |
Optimum parameters

- Extensive modeling and testing appear to support two needles, or one bipolar needle, using high voltage, 3kV, and multiple pulses

- These parameters allow for wider spacing of the needles, from 2 – 4 cm apart, does not have to be exact, with resultant regions of cell death in the 4-5 cm diameter range.
UC Discovery Grant
Lee, Loh, Kee + Oncologist + Pathologist

- 2 year funded study 9/07 to 9/09
- Implantation of VX2 tumor into liver of 60 New Zealand White rabbits
  - 1/3 control
  - 1/3 RFA
  - 1/3 IRE
- Imaging on multiple occasions
- Study nearing completion, in data collection stage
IRE-Nanoknife
Clinical Experience

Kenneth R Thomson MD, FRANZCR, FRCR
Professor & Director of Radiology
The Alfred, Melbourne, Australia
## Cancer

<table>
<thead>
<tr>
<th>METHOD OF TREATMENT</th>
<th>Cost</th>
<th>Risk</th>
<th>Collateral damage</th>
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<tr>
<td>Surgical removal</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Chemotoxotherapy (pre or post treatment)</td>
<td>+</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Receptor mediated chemotherapy (Herceptin)</td>
<td>+++</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Radiation therapy</td>
<td>++</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Brachytherapy</td>
<td>++</td>
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<tr>
<td>Chemo-embolisation (TACE)</td>
<td>+</td>
<td>+</td>
<td>+/-</td>
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<tr>
<td>Selective internal radiotherapy (SIRTEX)</td>
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<td>++</td>
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<tr>
<td>Ablative procedures (RFA, Microwave, Alcohol, Phenol)</td>
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<td>++</td>
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<tr>
<td>Irreversible Electroporation (Nanoknife)</td>
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<tr>
<td>Vaccination (cervical cancer)</td>
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Benefits of IRE

• Not dependent on cancer cell type
• Anywhere a needle can access
• Surrounding structures preserved
• No cavity for haemorrhage or infection
• Heat-sink from vessels irrelevant
• Quick < 1 minute compared to RFA 15-20 mins
• No “recovery time” for patient
• 1 day in hospital
Alfred Hospital Phase I study

- 18 patients with biopsy proven liver, kidney or lung cancer
- Failure of conventional therapy
- Six patients for each organ
- Primary end-point safety of technique in humans
- Secondary end-point satisfactory focal treatment of cancer
- Follow-up by clinical examination and radiologic imaging (CT)
- As of January 09 we have completed 7 liver patients, 2 lung patients and 2 renal patients and 2 lymph node metastases.

- Safety and feasibility has been established.
- We had over 1,000 patient contacts through phone and web in 2 weeks.
  - www.alfredradiology.org.au
Patient #1

- Unwilling to have further RFA
Immediately after Nanoknife – No pain Clear treatment zone
Two weeks later – liver regenerating
#1 One Month – Normal Ultrasound
Patient # 5

- Carcinoma of Endometrium 71 yo WF
- Lymph node metastasis behind aorta resistant to chemotherapy & radiotherapy
- No response to Radiotherapy and Chemotherapy
- Failed surgical removal
- Overnight stay with a 2 hour procedure
Patient #7

- 36 yo WF mother of 2 under 3 yrs
- Metastatic breast cancer
- Failed Chemotherapy
- Given 6-12 months by Oncologist
- Just wants “more time with the kids”
- Staged treatment
- Procedure time 2 hours
Nanoknife Procedure

• General anaesthetic
  – – BIS monitor, arterial line etc
• Muscle relaxant and machine ventilation
• Place needles under CT / US vision
• Activate pulse sequence (<60 seconds)
• Move needles to next site & repeat
• Remove needles & apply bandaid
• Wake up
• Go home next morning without any pain

• (Victorian State ALOS is 17.4 days – DRG Destruction of liver tissue)
Nanoknife Procedure

• What don’t you get?
  – Postoperative pain
  – Ablation “shock” syndrome
  – Ischaemic necrosis
  – Cavity formation
  – Fever
  – Long stay in hospital
  – Prolonged recuperation after
  – Drains
  – Wounds
  – Infection
Bipolar Needle – Focal disease or limited access

- 2 cm Treatment Zone @ 2,750 volts
- Lymph node metastasis
- Cancer of the uterus
Bipolar Needle – Focal disease or limited access

- 2 cm Treatment Zone @ 2,750 volts
- Lymph node metastasis
- Cancer of the uterus

3 punctures @ 1.5cm intervals
Unipolar Electrode Array - Planning

- Skin grid marked
- CT to check positions
Guidance

• CT more precise for larger lesions with Electrode Arrays
• US for liver and for Bipolar needle
  – (if there is an acoustic window)
Unipolar Electrode Array

- 1 - 2
- 2 - 3
- 3 - 1
- 2 - 4
- 4 - 3
- 1* - 3
- 1* - 4
- 1* - 2
- 2* - 1*
- 2* - 4
Patient #10

- 42 yo WM Father of three small children
- Right kidney removed for Renal Sarcoma 2005
- Metastasis in remaining kidney and liver
- Recurrence at original tumour site
- No response to radiotherapy and chemotherapy
Patient #10

- Unipolar electrode array (4 needles)
- Renal Metastasis treated at 1.5cm spacing
- CT guidance

Procedure 22/12 – Played football with his boys 25/12
Follow-up 3 weeks

- 52 x 51mm reduced to 38 x 39mm at IMA level
- Treatment for renal bed recurrence and liver planned
Massive Hepatoma

• 71 Chinese male with Hep B& C Cirrhosis
• Co-incident Bladder TCC
• Rejected by Urologists because of liver cancer
Planning Error – Skip lesions
Treatment extended same session
Metastatic melanoma

- 46 yo WF
- Single PET avid node
- Failed XRT
- Paraneoplastic Myositis
- No pneumothorax or bleeding
Patient #13

- 71 yo WM Prostate cancer 2001
- NSTEMI with 5 coronary stents 2002
- Colon cancer 2003 surgery with XRT and chemotherapy
- 2005 has 6 metastases in both lungs removed by thoracotomy
- 2006 Radiowave thermal whole body treatment for more metastases
- 2008 April multiple new metastases both lungs
Patient #13

- Bipolar Electrode 30 activations
- No haemoptysis or pneumothorax
- No pain
Pre & Post IRE
Final Thoughts

• These patients were “rejects” from conventional care
• Many were too big for RFA/Microwave/Cryotherapy/Cyberknife
• The minimal morbidity of the Nanoknife is remarkable

• The ability to work right up to the wall of the aorta or great veins without damage and the ability to treat lesions near to or involving a nerve plexus has changed the paradigm for focal cancer treatment.

• Possible Limitations
  – Cardiac arrhythmia without synchronisation
  – Electrode track tumour “seeding”
  – Possibility of pancreatic duct leakage
  – Electrical effect on brain
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