Clinical/Surgical trials that will change my practice

Mr Jim M Adshead

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Lister Hospital

What's changed and where do I feel we are clutching at straws?

- Regional Specialist Renal MDT with renal oncologist
- Robotic Partials replaced open
- Biopsy more and more small renal masses
- Large group of surveillance patients
- Percutaneous CT Cryotherapy

- Cytoreductive nephrectomy in mRCC?
- Metachronous Metastectomy?
- Will the partial survive?

Easy-
There are only 2 we can recruit to

* Carmena
  * the role of nephrectomy in mRCC
* Surtime
  * The timing of nephrectomy in mRCC

Easy-
There are only 2 we can recruit to

* Carmena	Closed in UK
* Surtime	Closed in UK

Do we need to take the kidney out when mets will be left behind?

* Radical nephrectomy should not be performed with the aim of inducing spontaneous remission—only 0.8% of patients treated with radical nephrectomy alone achieve this outcome
* Can palliation alone justify nephrectomy?
* In the Alpha interferon era the EORTC and SWOG studies showed a 6 month survival benefit for cytoreductive nephrectomy
* What is the answer in TKI era?

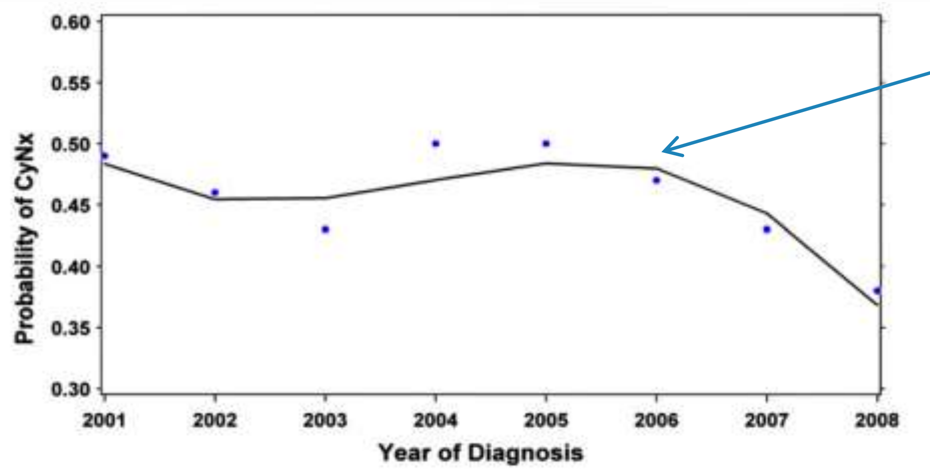
Maybe we think we already know the answer?

World J Urol (2013) 31:1535–1539
DOI 10.1007/s00345-012-1001-3

ORIGINAL ARTICLE

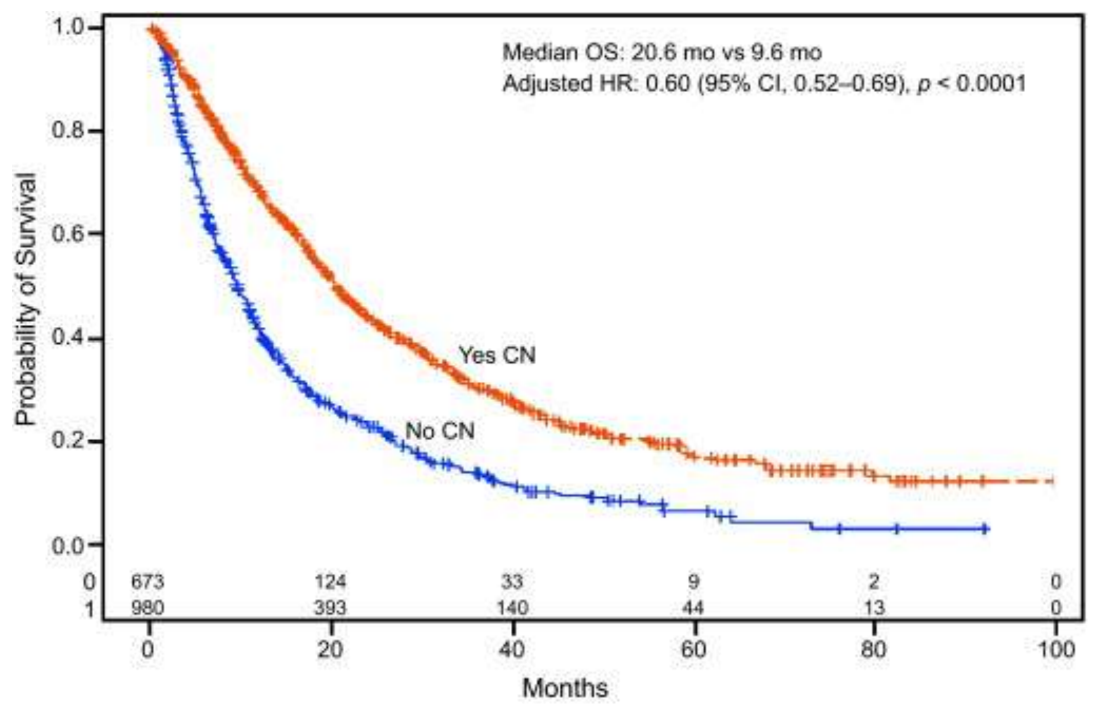
Cytoreductive nephrectomy for metastatic renal cell carcinoma in the era of targeted therapy in the United States: a SEER analysis

Che-kai Tsao · Alexander C. Small · Max Kates · Erin L. Moshier · Juan P. Wisnivesky · Benjamin A. Gartrell · Guru Sonpavde · James H. Godbold · Michael A. Palese · Simon J. Hall · William K. Oh · Matthew D. Galsky



Introduction of TKIs

Daniel et al, European Urology, 2014



- **1633 matched retrospective**
- **Half had prior Nephrectomy**
- **Survival post starting TKI**
- **NOT RANDOMISED**

Cytoreductive Nephrectomy in Patients with Synchronous Metastases from Renal Cell Carcinoma:

International Metastatic RCC Database Consortium

Carmena Study- role of Nephrectomy

* A multinational, prospective, randomized trial is underway to answer this question (CARMENA :NCT00930033).
* Patients with untreated metastatic clear-cell RCC and a good performance status (ECOG PS 0 or 1), are randomly assigned to either nephrectomy followed by sunitinib or to sunitinib alone.
* The primary endpoint is overall survival
* 1,000 patients.
* Completes 2016
* Patients in the sunitinib-only arm can have palliative nephrectomy later in the disease process if deemed necessary for symptomatic control. In the meantime nephrectomy should be recommended, except perhaps in those patients with risk for poor prognosis ie less than 12 month survival expected

What have the French done for us?

Managed to recruit 250+ to Carmena

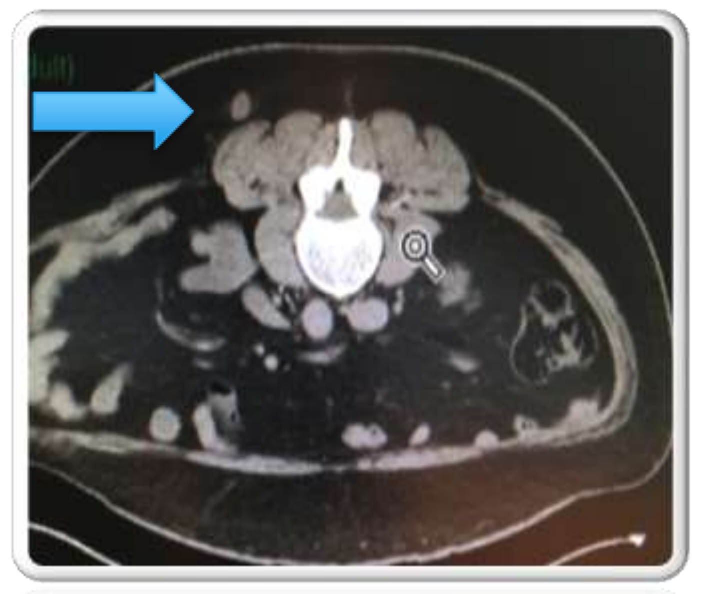
UK arm closed as only 14 recruited

What are we saying in our clinics?

History of the Renal MDT

* Chemo-resistant tumour
* Renal discussed in local MDT
* MDTs have been surgeon dominated
* New renal sMDTs springing up across the country
* Specialist oncology input increasing
* SORCE (1656) and RADICALS (1900) adjuvant treatment post surgery have recruited very well
* Do we struggle to recruit to trials that we perceive as a threat?
  * Surgeon outcome data and volume
  * Spread and variety of treatments rather than number of ops
* SURTIME UK arm closed too with around 10 UK contributions

What about metastectomy?



Metastectomy has never been through a randomized control trial

Complete resection of isolated metastases is associated with 5-year survival rates of between 35 and 60%.

However, there is no “definitive” proof that the surgical intervention itself, as opposed to patient selection factors and the natural history of renal cancer, is responsible for the observed outcome

Could Radiotherapy Return?

* Professor Martin Gore (Royal Marsden)
  * Kidney Cancer Association's Ninth European International Kidney Cancer Symposium in Dublin
  * His 10 year predictions Cyberknife and proton beam

Ablation in the Outpatients

Comparison of Partial Nephrectomy and Percutaneous Ablation for cT1 Renal Masses

R. Houston Thompson[a], Tom Atwell[b], Grant Schmit[b], Christine M. Lohse[c], A. Nicholas Kurup[b], Adam Weisbrod[b], Sarah P. Psutka[a], Suzanne B. Stewart[a], Matthew R. Callstrom[b], John C. Cheville[d], Stephen A. Boorjian[a], Bradley C. Leibovich[a]

The Journal of Urology

Available online 14 August 2014

In Press, Accepted Manuscript — Note to users

Single-fraction radiosurgery for the treatment of renal tumors

Michael Staehler[1], Markus Bader[1], Boris Schlenker[1], Jozefina Casuscelli[1], Alexander Karl[1], Alexander Roosen[1], Christian G. Stief[1], Axel Bex[3], Berndt Wowra[2], Alexander Muacevic[2]

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- 40 patients SRM <4cm not suitable for surgery
- 29 RCC 11 TCC
- 26 month follow up
- No progression of lesions
- No TCC detected in all 11 at URS
- No mets and no deterioration in creat clearance
- No restrictions to anatomy
- 19/40 complete ablation on imaging
- Needs longer follow-up

CASE REPORT JSLS

Salvage Robot-Assisted Partial Nephrectomy for the Management of Renal Cell Carcinoma Following Failed Stereotactic Radiotherapy

Michael A. Gorin, MD, Vladislav Gorbatiy, MD, Charles Glenn, MD, Samir P. Shirodkar, MD, Scott M. Castle, MD, Merce Jorda, MD, PhD, Raymond J. Leveillee, MD

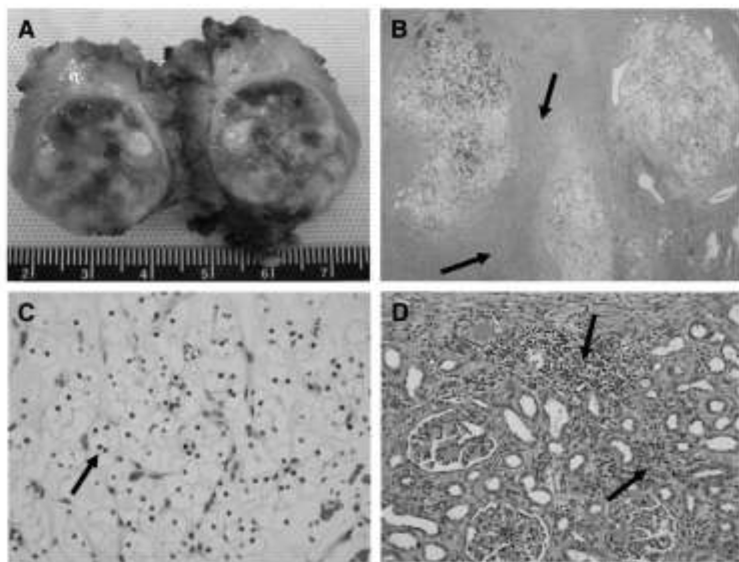


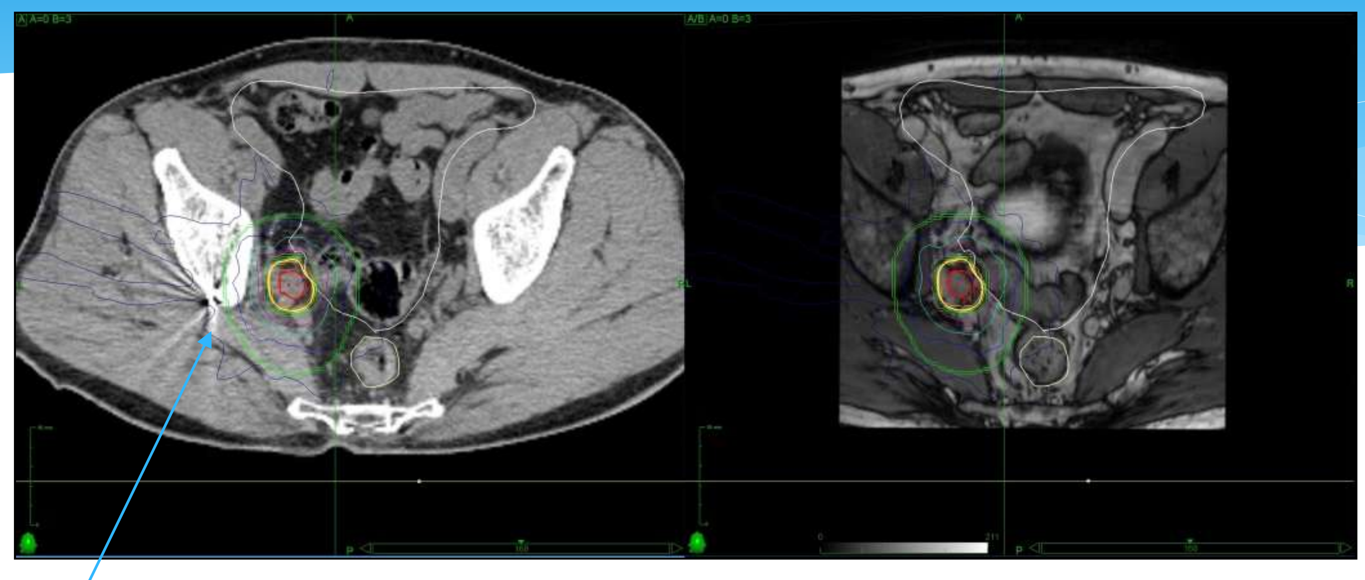
Figure 3. (A) Bisected partial nephrectomy specimen with well-circumscribed, variegated 2.2-cm neoplasm. (B) Renal cell carcinoma with areas of extensive hyalinization (arrows), H&E 4X. (C) Tissue adjacent to fiducial marker showing viable renal cell carcinoma, conventional (clear cell) type, Fuhrman nuclear grade 1 (arrow), H&E, 40X. (D) Renal parenchyma with nonspecific chronic inflammation (arrows), H&E, 20X.

Does Cyberknife ablate mets?-Mr DB

* 66 year
* PSA 33
* RALP + Ext PLND dissection 2011
* T3b neg margins
* 2/24 nodes involved but PSA <0.003
* Opted for Immediate prostate bed radiotherapy
* No hormones
* PSA relapse

PSA relapse	Sept 2013	PSA 1.5
	Nov 2013	PSA 3.2
	Solitary node on total body MRI	
	Dec 2013	Cyberknife

Does cyberknife ablate?-Mr DB



Fucidial marker in situ

30 Gy /3# stereotactic radiotherapy plan

* PSA relapse

Sept 2013	PSA 1.5
Nov 2013	PSA 3.2
May 2014	PSA<0.05

Could cyberknife replace metastectomy?

Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Merina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Christopher M Nutting, Peter J Ostler, Nicholas J van As

Renal metastatic site

3 treatments in an outpatient setting

- Lung/adrenal/renal bed
  - 30 pts -only 2% progressed with 52 mths FU
- Adrenal
  - 90% 2 year local control/ablation
- Bone
  - 149 pts 70-80% local control 15 months FU

Oligometastases Trial

STUDY PROTOCOL **Open Access**

Stereotactic ablative radiotherapy for comprehensive treatment of oligometastatic tumors (SABR-COMET): Study protocol for a randomized phase II trial

David A Palma[1*], Cornelis J A Haasbeek[2], George B Rodrigues[1], Max Dahele[2], Michael Lock[1], Brian Yaremko[1], Robert Olson[3], Mitchell Liu[3], Jason Panarotto[4], Gwendolyn H M J Griffioen[2], Stewart Gaede[1], Ben Slotman[2] and Suresh Senan[2]

SURAB Study- A randomised study comparing ABlation with active SURveillance, in the management of incidentally diagnosed small renal tumours: a feasibility study

Chief Investigator: Mr Naeem Soomro

Sponsor: Newcastle upon Tyne Hospitals NHS Foundation Trust

Funder: NIHR-HTA (11/107/01)

NIHR CRN adopted

Study summary

* Multi-centre feasibility study
* Randomised controlled trial
* Surveillance vs. Ablation 1:1 ratio at each site
* Recruitment target: 60 patients – with ~ 8 patients to be recruited per site

Primary objective

"The aim of this study is to establish whether a future definitive trial comparing active surveillance with ablative treatment for small kidney cancer is feasible".

Sites approached

* Newcastle, David Rix
* Southampton, David Breen
* Leeds, Tze Wah
* Royal Free, Rowland Illing
* Bristol, Frank Keeley
* Stevenage, Jim Adshead
* Glasgow, Gren Oades
* Oxford, Mark Sullivan
* St Georges, Chris Anderson
* Sunderland, Stuart McCracken

One RCT has managed to recruit

JOURNAL OF CLINICAL ONCOLOGY

Official Journal of the American Society of Clinical Oncology

Randomized Controlled Trial of Expressive Writing for Patients With Renal Cell Carcinoma

JCO Mar 1, 2014:663-670; published online on January 27, 2014

- N=277
- Randomised to EW or NW
- Stat signif improvement in cancer related symptoms

MasterCard

there are some things money can't buy.
for everything else there's MasterCard.

* TKIs — £75 per day
* Cyberknife — £15,000
* Pencil and pad — £2.56
* Surgical Trial recruitment — Priceless