Organ sparing treatment in MIBC:

Robot assisted laparoscopy & Interstitial Radiotherapy – brachytherapy

Curie - daVinci connection

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Intuitive: International proctor

Electa: Scientific collaboration

NO patents
NO shares
NO other financial benefits
Curie - daVinci connection

Arnhem - the Netherlands
Radical Cystectomy in MIBC

- Gold standard, > 60 yrs experience
- Still challenged:
  - 5y survival not 100% (understatement)
  - peri-operative mortality 1.5 – 4.2%
  - up to 67% complications
  - QOL after urinary diversion?
  - sexual functions compromised

→ Multimodality treatments
→ Bladder sparing
Bladder sparing strategies in MIBC

- TUR + Partial Cystectomy alone
  - Undertreatment

- Chemo included strategies
  - TUR + systemic chemo
  - TUR + partial cystectomy plus chemo
  - TUR + chemo-radiation protocols
  - Systemic side-effects

- TUR + ExtBeamRT – surgery - Interstitial RT
  - Best local control
Chemo included strategies

Mak RH, Hunt D, Shipley WU
Long-term outcomes in patients with muscle-invasive bladder cancer after selective bladder-preserving combined-modality therapy: a pooled analysis of Radiation Therapy Oncology Group protocols 8802, 8903, 9506, 9706, 9906, and 0233
J Clin Oncol. 2014 Dec 1;32(34):3801-9

Arcangeli G, Arcangeli S, Strigari L
A systematic review and meta-analysis of clinical trials of bladder-sparing trimodality treatment for MIBC
Crit Rev Oncol Hematol. 2015 Apr;94(1):105-15
Partial Cystectomy

- Minority patients suitable candidates → 5.8 - 18.9 %
- Normal functioning bladder/good capacity
- 1-2cm extra margin
- No CIS

→ Local recurrence rate 37-78%
→ Survival rates 35-70%

Holzbeierlein JM, Lopez-Corona E, Bochner BH: Partial cystectomy: a contemporary review of the Memorial Sloan-Kettering Cancer Center experience and recommendations for patient selection
J Urol. 2004 Sep;172(3):878-81

Kassouf W, Swanson D, Kamat AM: Partial Cystectomy for Muscle Invasive Urothelial Carcinoma of the Bladder: A Contemporary Review of the M. D. Anderson Cancer Center Experience
J Urol. 2006 Jun;175(6):2058-62

Knoedler J, Frank I: Organ-sparing surgery in urology: partial cystectomy
See comment in PubMed Commons below Curr Opin Urol. 2015 Mar;25(2):111-5
History
Interstitial Radiotherapy
- US /NY: Barringer 1915, only IRT (Radium)

- Europe 50’s (Cesium)
  - France, Belgium, Netherlands
- Rotterdam: vd Werf-Messing:
  - Introduction EBRT:
    - Downstaging, Lymphnodes, prevention ent mets

- Arnhem, NL (EBRT + Iridium HDR)
  → Minimal invasive surgery, robot assisted
Literature
interstitial radiotherapy
Iridium publications (Fr, Be, NL)

Rozan R, Albuisson E, Donnarieix D
Interstitial iridium-192 for bladder cancer (a multicentric survey: 205 patients)

Pernot M, Hubert J, Guillemin F
Combined surgery and brachytherapy in the treatment of some cancers of the bladder
(partial cystectomy and interstitial iridium-192)
*Radiother Oncol.* 1996 Feb;38(2):115-20

Soete G, Coen V, Verellen D
A feasibility study of high dose rate brachytherapy in solitary urinary bladder cancer

Hoffstetter S, Hubert J, Guillemin F
Interstitial brachytherapy in infiltrating cancer of the bladder. The Nancy experience
*Cancer Radiother* 1998 Apr;2 Suppl 1:54s-61s

van Poppel H, Lievens Y, van Limbergen E
Brachytherapy with Iridium-192 for Bladder Cancer
*Eur Urol.* 2000 May;37(5):605-8

de Crevoisier R, Ammor A, Court B
Bladder-conserving surgery and interstitial brachytherapy for lymph node negative transitional cell carcinoma of the urinary bladder: results of a 28-year single institution experience
*Radiotherapy and Oncology* 72 (2004) 147-157
Recent publications

  - Brachytherapy after external beam radiation and limited surgery preserves bladders for patients with solitary pT1-pT3 bladder tumors

  - Bladder function preservation with brachytherapy, external beam radiation therapy and limited surgery in bladder cancer patients: long term results
Recent publications

- vdSteen-Banasik: Radiother Oncol, nov 2009
  
  - Brachytherapy versus cystectomy in solitary bladder cancer: a case control multicentre, east-Netherlands study
Conclusions literature

- Curation in well defined cases
- Survival comparable with cystectomy
- Considerable toxicity
- Intensive collaboration
- Only few centers perform this technique
- N>1000 patients worldwide
Treatment protocol

cT2-3a, cN0, solitary tumor, no CIS
Treatment protocol

- TUR-Bladder tumor: ‘radical’
  - cT2-3a, cN0, solitary tumor, no CIS
- 2-4 weeks post TUR-B: MRI and Cystoscopy
Treatment protocol

- 4-6 weeks post TUR-B:
  - EBRT: 20 x 2Gy in 4 weeks
- 1 week after EBRT surgery:
  - Lymphnode dissection +/-
  - Partial cystectomy +/-
  - Placement brachytherapy catheters (source carrier tubes)
- Interstitial Radiotherapy
  - Total 10 x 2,5 Gy (HDR)
  - 3 per day
How it works?
OPEN Surgery
OUR GOAL

Organ preservation
Improve toxicity
Enhance effectivity

2009: Laparoscopic surgery
2010: ROBOT-assisted laparoscopy
3D monitors
real-time virtual & augmented reality
Arnhem: Minimal invasive surgery since 2009

- Lithotomy & Trendelenburg position
- Simultaneous Laparoscopy and Cystoscopy
- 2010 start daVinci Si:
  - Side docking, TilePro function
Arnhem-needle → Luneray®
View in console
Needle handling
Positioning clips
Robot assisted partial cystectomy
No kinking
No loading errors
Homogeneity Index 57%
Overdose Index 20%
Removal catheters
Follow-up

Year 1: 3m  CYSTOSCOPY AND CYTOLOGY
Year 2: 4m
Year 3: 5m
Year 4: 6m

PET-CT or MRI when indicated (8/65)
Our results
Population, MIS + HDR

- N = 58 with pT2 (mean 2.8 cm)

- Partial cystectomy in 17 cases
  - Diverticulum 3
  - Urachus 4
  - Distal ureter 2
  - Thick residual tumor: 8

- Lymphnode dissection 8 (1+)
Oncological results, MIS + HDR

- mean FU 2.5 yrs (0.4-5.6)
- 4 in field recurrence; 4 RC
- 6 sec bladder tumor; 3 RC
- 6 distant mets
  - 3 had in field recurrence tumor
  - 3 cases without local recurrence
- Local Cure 81%
- DSS 86%
## Toxicity CTCAE v4

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Open vs Robot
series Rijnstate

**OPEN**
- N=77
- Age: 68yr (41-87)
- FU: 6yr (0-24)
- Hosp: 16d (6-90)

**ROBOT**
- N=58
- Age: 70yr (48-86)
- FU: 2.6yr (0-5.9)
- Hosp: 4-5d (4-17)
Open vs Robot results

Vd Steen, Smits et al:
5 years of laparoscopic (RA) implantation for HDR brachytherapy in solitary bladder tumor
Submitted sept 2015 Radiother Oncol
Conclusion 1

- Minimal invasive surgery feasible
- Improved treatment quality
- Reduced toxicity
- Reduction LOS 16 → 5 days
- Oncological results as in open surgery
- Very good functional results
- Rijnstate serie promising
- Worldwide centres now starting
Future perspectives

- Intens multidisciplinary collaboration mandatory
- Increasing awareness bladder preservation
- Increasing number patients could benefit
- Need multicentre randomized studies
  - Partial cystectomy
  - Lymphnode dissection?
  - Combination with chemotherapy?
- Implementation in international guidelines
In the long history of human kind, those who learned to collaborate and improvise most effectively have prevailed.

Ch. Darwin