



Bladder Brachytherapy- - ready for a change?

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OUTLINE

1. Compare bladder sparing strategies vs. cystectomy for muscle invasive B.cc.
2. BT in the bladder sparing approach
3. Bladder Brachytherapy (BBT) technique

Driving force= bladder preservation

Radical (total) cystectomy + ... ♀ , ♂

à DSS10 = 75-(85)% pT(1)-2, 30-35% pT3-4N0/pN+

à 10 yOS \approx 50 % for pT2No, 25% for pT3-4 or pN+

à "Major" complications: \sim 50% (acute & late)


à 2-7 % per/ postop. Mortality

But TCC is a Radio & chemo-sensitive cancer!

(\rightarrow pCR 40-50 % after preop RT or after na.CT)

Bladder preservation attempts (BPA)

1) concom. Radio-Chemotherapy = RCT (* 3 M*)
maximal TURB → neoadj CT → RCT (< 15% of pts)
Cystectomy ← ~ 25% (10% UK; 35% US)



2) Preop. short EBRT + Partial cystectomy + Interstitial postop. Brachytherapy (*m3M*= no chemo)
- highly selected T2 patients (< 5% of pts)

3) < 3M (TURB alone or + chemo) < 10 % of pts
+ RT =.... BT only)

BPA vs. radical cystectomy

- no randomised trials!
- SPARE trial (CRUK/07/011)- failed to accrue
(Moynihan C et al, Trials 2012; 13: 228)

à Large cohort studies, prospective & NR

Biases: pT vs. cT;

(+) vs. (-) neoadj/ c/ adj chemo..

BPA vs. radical cystectomy

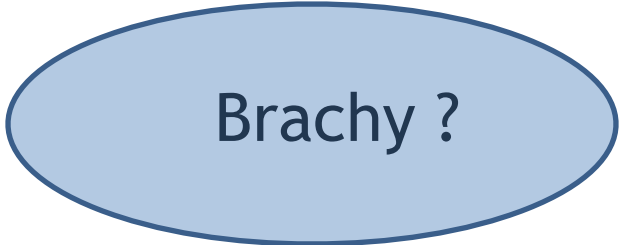
Ref	nb. Pts.	5y OS (%)	10 Y OS (%)
Radical Cystectomy		CSS = +15%	pT2No: 45 %;
Madersbacher (JCO2003)	320 (37 % ≥ pT3)	T1-2: 65 T3: 40 %	T1-2:45 T3:30 %
Hautmanm (Eur Urol 2012)	560 (28 % ≥ pT3)	T2: 55 T3: 45	T2: 44 T3: 30
3M (RCT)			cT2N0: 43 %;
Rodel (JCO 2006)	331 pts	54	36
Efstathiou [splitRT] (Eur Urol 2012)	348 (35 % ≥ T3)	52	35
m3M (EBRT+TUR/PC +BT)			cT2N0: 45 %
Koning (Ann Oncol 2012)	1040 (10% ≥ T3)	62	44
De Crevoisier (R&O2004)	58 (12 % ≥ T3)	T1:69; T2 : 60; T3: 38	
Aluwini (IJROBP 2014)	192 (6.2 % T3)	65	46

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METS

Un-met needs

1. Improve distant control à (Neo)/ Adjuvant chemo ?
 - 35-50 % distant mets
2. **Improve local control** à 
 - 35-50 % bladder "rec"
 - Multifocality / new T
 - Superficial rec. (1/2)
 - **BLADDER SPARING**

..... "Focal therapy" ?
(treat only the dominant lesion)
3. **RANDOMIZED TRIALS** → Uniform toxicity scales
 - multidisciplinary Uniform geriatric eval.

RCT- what doses of RT?

- EBRT: 45Gy/ 25fr/ 5 wks + boost < 20 Gy.
(boost1 → 54 Gy; boost 2 → 64.4 Gy) → LC5:65%
 - (30)-40 Gy EBRT + 30- (40 Gy) BT → LC5= 80%
 - 0 Gy → no loss in OS but ~ 33 % in bladder preservation vs. Chemo alone !
- RADIATION is important for bladder sparing

Candidates for bladder 3M

▶ "Ideal": **MOTIVATED PATIENT**

T2N0, no HNF, no CIS, G1/G2, LVI(-), with macroscopically completely resected T. (max TURB!), no stromal prostate invasion*

+ for brachy: solitary T (also T1G3?)

< 5 cm

without bladder neck-invasion

Bladder brachytherapy

à High dose, small volume

à Only + SURGERY (TURB/ Partial Cy+ LND)

à Usually as a complement to EBRT

- most of the BT series= preop EBRT \approx 10 Gy hF (not needed after TUR or robotic/ lap PC!) \rightarrow BT only(?)

- Dutch: = real "boost" (EBRT 40Gy/20fr + 25-30 Gy BT, LDR or PDR)

Not suitable for bladder sparing 3M but potential for BT?

- active inflammatory bowel/ chronic pelvic inf
- severe irritable bladder
- previous pelvic RT or extensive Surgery

"New indications" for Brachy?

- Only BT (without EBRT)?
 - good responders after na chemo?
 - mark the initial T limits (metallic clips)
 - no treatment on LN (?)

- 4M (TURB/PC+ chemo+ EBRT + BT)?
 - optimal sequence ?

Toxicity = PRO for BT

Toxicity

NCI- C (Coppin, JCO, 1996): T3 → RT vs. RCT/ Cisplatin Better long-term local control (47 vs. 67%), same OS!

UK (James, NEJM 2012): - 360 p.

→ RCT/ 5FU-MMC vs. RT: Better Loco-reg DFS; OS=!

--> **G3-4 toxicity:**

- acute = 36 vs. 27 % (p=0.07)

- late = 8.3 vs. 15.7 % (NS)

(GU= 7.5 %, GI= 0.8 %,)

----> death due to treatment < 1%

Cystectomy

30-35 %

15- 20 %

≈5 %

Brachy: acute: 10-15 %

late*: GU= 5.7 %; GI = 1 %

(* Aluwini, et al. IJROBP 2014; 88: 611)

Brachy toxicity

ACUTE

- thromboses
- infections
- impaired wound healing
- fistula (French multicenter

8 vs. 22 % PC+BT vs. TURB +BT)

LATE

- hematuria (20%)
- lithiasis (7-17%)
- ulceration/ fistula (2-3%)
- ureter stenosis (1%)
- severe chronic radiocystitis (0.6%)

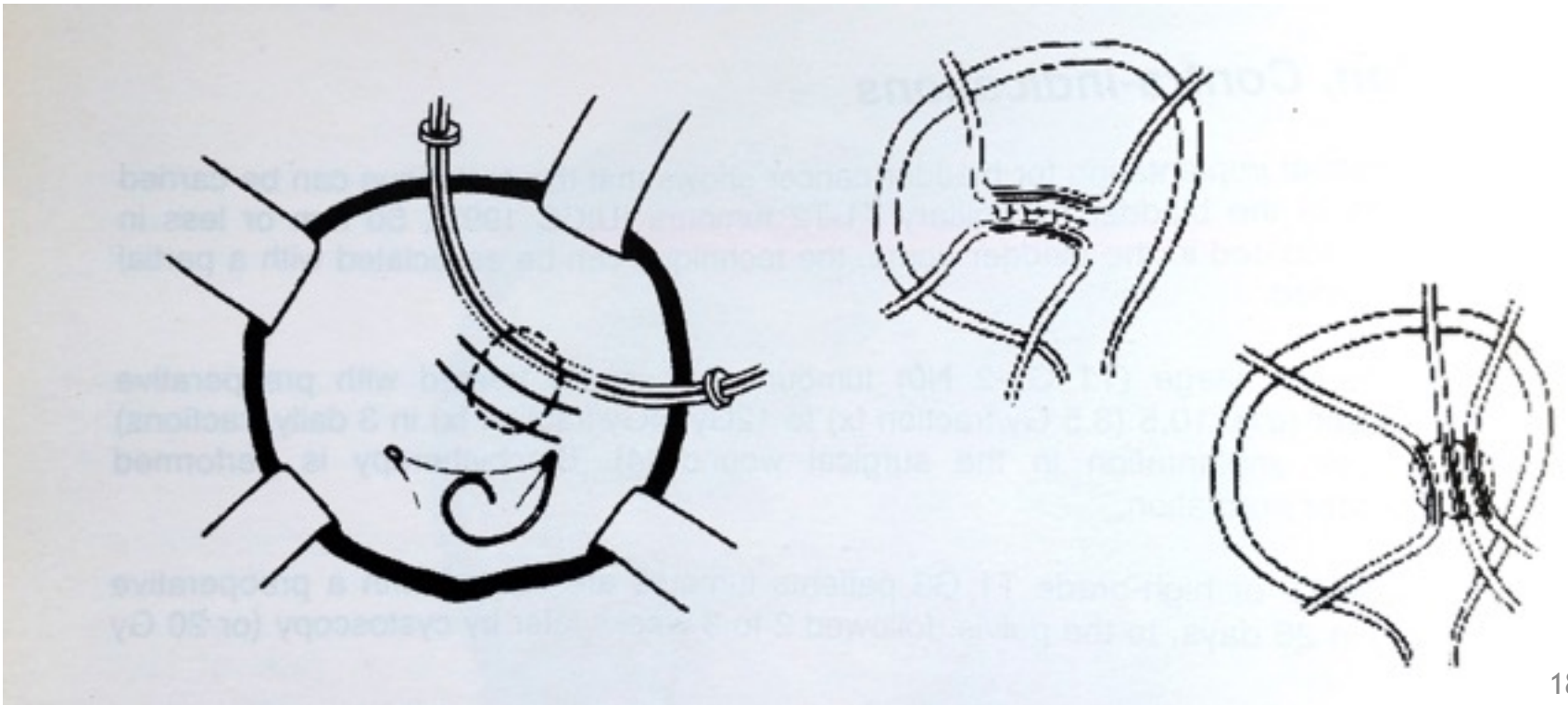
Brachy technique (LDR, PDR)

- Perop. (after open PC + LND)
 - lap/robo → after TURB/ after na CT/ after RCT
 - keep LN treatment in mind!
 - clips in the B. Wall to mark the T./ scar limits.
- General/ peridural anesthesia
- Foley +/- Suprapubic cath
- Start BT only after D4 (get the path full report → no BT?)

Brachy technique

PTV= CTV = scar/ T. Bed/ Residual tu + 10 mm

- full thickness of bladder
- plastic tubes in the outer half of the B. wall
- exceed T limits by 10 % each side



Pro & Cons for BT

- PRO
 - at least as good as any other curative option* (selected pts!)
 - low toxicity (vs. *)
 - much shorter than EBRT
 - feasible as re-irradiation/ other EBRT contraindic.
 - ensures real multidisciplinary
- CONS
 - Highly selected pts
 - Very scarce HDR experience
 - Logistic Complicated

READY for a Change?

1. OK BT for highly selected pts in multidisciplinary high tech environment.
 2. Explore new indications (Only BT → 4M)
 3. Gather/ share HDR experience
- Collaborative international clinical studies₂₀