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 ≈ 50% for pT2No, 25% for pT3-4 or pN+

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

à 2-7% per/postop. Mortality

But TCC is a Radio & chemo-sensitive cancer!

(⇒ pCR 40-50% after preop RT or after na.CT)
Bladder preservation attempts (BPA)

1) concom. Radio-Chemotherapy = RCT (* 3 M*)
maximal TURB $\rightarrow$ neoadj CT $\rightarrow$ 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

<table>
<thead>
<tr>
<th>Ref</th>
<th>nb. Pts.</th>
<th>5y OS (%)</th>
<th>10y OS (%)</th>
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Un-met needs

1. Improve distant control
   - 35-50 % distant mets

2. Improve local control
   - 35-50 % bladder “rec”
   - Multifocality / new T
   - Superficial rec. (1/2)
   \[\rightarrow \text{BLADDER SPARING}\]

3. RANDOMIZED TRIALS
   - multidisciplinarity

\[\rightarrow \text{à (Neo)/ Adjuvant chemo ? à \text{Brachy ?}}\]

\[\text{à \text{ Brachy ? \text{“Focal therapy” ? \text{(treat only the dominant lesion)}}}}\]

\[\rightarrow \text{à \text{…. Uniform toxicity scales \text{…. Uniform geriatric eval.}}}\]
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

- High dose, small volume

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

- Usually as a complement to EBRT
  - most of the BT series = preop EBRT ≈ 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:急性: 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 multidisciplinarity

• 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 studies