ElectroMotive Drug Administration (EMDA)

Jonathan Borwell

- Local anaesthesia of the bladder
- Intravesical treatment of interstitial cystitis
- Intravesical treatment of bladder cancer
- Intravesical treatment of recurrent, infective cystitis
- Intravesical treatment of hyperreflexic bladders
- Intraprostatic treatment of non-specific prostatitis
- Intraprostatic treatment of infective prostatitis
- Peyronies Disease

- EMDA combines several interactions
  - Iontophoresis
  - Electroosmosis/Electrophoresis
  - Electroporation
    - All of which are responsible for EM transport of drug molecules in an electric field across biological membranes into underlying tissues.

Urothelium	PD	46.6
P=<0.0001	EMDA	170.0
Lamina Propria	PD	16.1
P=<0.0001	EMDA	65.6
Muscularis	PD	1.9
P=<0.0005	EMDA	15.9

MMC concentrations in bladder tissue (PD vs. EMDA)
All bladder sections remained viable and the chemical structure of MMC was unaffected.

Cancer Research, 1999 59(19):4912-4918

Di Stasi et al. Lancet Oncol; 7: 43-51

- All patients underwent TUR(BT)
  - 212 patients
  - Multi-centred
  - Stage pT1 – All grades +/- cis
  - Treatment initiated 3/52 post TUR

- "BCG-induced inflammation increases the permeability of the bladder mucosa, such that Mitomycin can reach the target tissue more easily."

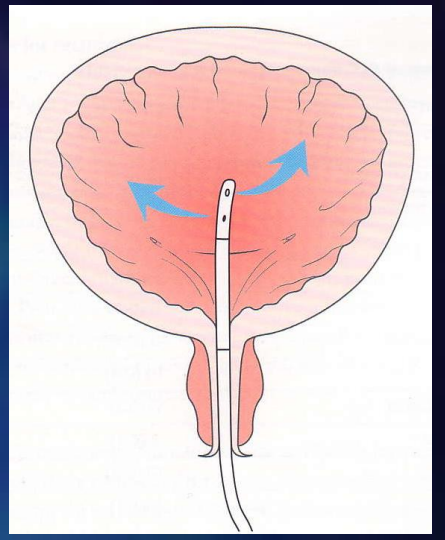
- BCG vs. sequential BCG and EMDA MMC
  - BCG x 1 Weeks 1 and 2 (n=107)
  - MMC x 1 Week 3
    - Repeated for 3 cycles
    - Then monthly infusions i.e. MMC/MMC/BCG for 9 months

Summary of Di Stasi regime

- Week 1 BCG
- Week 2 BCG
- Week 3 MMC
- Week 4 BCG
- Week 5 BCG
- Week 6 MMC
- Week 7 BCG
- Week 8 BCG
- Week 9 MMC
- Month 3 MMC
- Month 4 MMC
- Month 5 BCG
- Month 6 MMC
- Month 7 MMC
- Month 8 BCG
- Month 9 MMC
- Month 10 MMC
- Month 11 BCG

- In addition those having Mitomycin were
  - Given PO $NaHCO_3$ 3 doses
  - Fluid restriction 2 hours pre treatment
  - Current protocol suggests 2g $NaHCO_3$ in 30mls water

Superficial Bladder Cancer: *Treatment*



Å Di Stasi *et al*

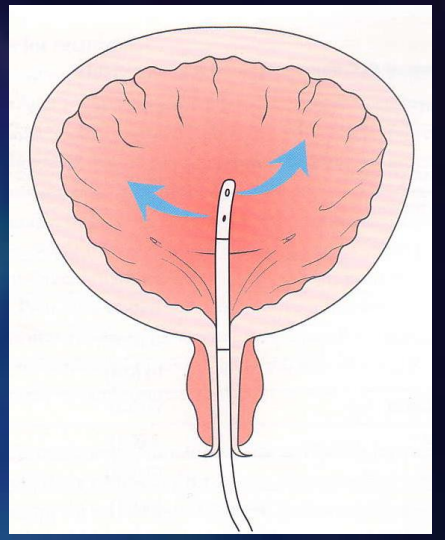
pT1 disease 212 Patients randomised to

BCG, 2 hrs, 1/week for 6 weeks (n=105)

v.s.

BCG, 2hrs, 1/week for 2 weeks followed by
40 mg EMDA mitomycin (20 mA for 30 min) x1
for three cycles (n=107).

Superficial Bladder Cancer: *Treatment*



Å Di Stasi *et al*

Median follow-up 88 months (IQR 63-110)

BCG & EMDA mitomycin vs BCG alone

Significantly higher disease-free interval

69 months vs 21 months

- 40mg MMC/ 100mls Water
- Catheterised with electrode catheter
- Bladder lavage with sterile water and drained
- Drug instilled
- Machine initiated (40-60 mA/s to a maximum of 20mA pulsed electric current)
- Treatment lasts 25-30 minutes
- Bladder drained
- Catheter removed


PHYSIONIZER
by PHYSION
ON
OFF
+
−
ENT
RST
START
STOP

Results

- Sequential BCG/EMDA MMC had higher disease-free interval than BCG alone arm.

  Mean FU = 88 months
- Lower recurrence (41.9% vs. 57.9%)
- Lower progression (9.3% vs. 21.9%)
- Lower mortality- disease specific

  (5.6% vs. 16.2%)

  Localised side effects; no systemic effects. Side effects comparable in both arms.

Pre-Operative EMDA MMC

- 167 pts randomised to 3 arms
  - Passive post-op 1 shot MMC (n=56)
  - Pre-Op EMDA MMC (n=54)
  - TUR(BT) alone (n=57)

67%	RR	TUR alone
53.6%	RR	Passive MMC
37%	RR	Pre-operative EMDA MMC

Di Stasi et al, Abstract 1707, EAU, 2008

Cost Implications

- EMDA Machine (approx. £5500)
- Electrode catheters (approx. £130/each)
- Other consumables incl. pads (approx £10)
- Resources – Treatment lasts 30m although set up, treatment etc 60m