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.
<table>
<thead>
<tr>
<th>Layer</th>
<th>Treatment</th>
<th>Concentration (PD)</th>
<th>Concentration (EMDA)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urothelium</td>
<td>PD</td>
<td>46.6</td>
<td>EMDA</td>
<td>170.0</td>
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<td></td>
<td>EMDA</td>
<td></td>
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</tr>
<tr>
<td>Lamina Propria</td>
<td>PD</td>
<td>16.1</td>
<td>EMDA</td>
<td>65.6</td>
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<td></td>
<td>EMDA</td>
<td></td>
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</tr>
<tr>
<td>Muscularis</td>
<td>PD</td>
<td>1.9</td>
<td>EMDA</td>
<td>15.9</td>
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<tr>
<td></td>
<td>EMDA</td>
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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

<table>
<thead>
<tr>
<th>Week 1</th>
<th>BCG</th>
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<tbody>
<tr>
<td>Week 2</td>
<td>BCG</td>
</tr>
<tr>
<td>Week 3</td>
<td>MMC</td>
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<tr>
<td>Week 4</td>
<td>BCG</td>
</tr>
<tr>
<td>Week 5</td>
<td>BCG</td>
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<tr>
<td>Week 6</td>
<td>MMC</td>
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<tr>
<td>Week 7</td>
<td>BCG</td>
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<tr>
<td>Week 8</td>
<td>BCG</td>
</tr>
<tr>
<td>Week 9</td>
<td>MMC</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Month 3</th>
<th>MMC</th>
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<tr>
<td>Month 4</td>
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<tr>
<td>Month 5</td>
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<tr>
<td>Month 6</td>
<td>MMC</td>
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<td>Month 7</td>
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<td>Month 8</td>
<td>BCG</td>
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<tr>
<td>Month 9</td>
<td>MMC</td>
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<tr>
<td>Month 10</td>
<td>MMC</td>
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<tr>
<td>Month 11</td>
<td>BCG</td>
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</tbody>
</table>
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) x 1
t 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
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

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