A prospective clinical trial of intra-operative tissue oxygenation measurement and its association with anastomotic leak rate after Ivor Lewis esophagectomy

Supported by U-54 Award

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Surgical Anastomoses

• All surgical resections and reconstructions require restoration of blood supply

Intestinal anastomosis

Coronary anastomosis

WiPOX – Wireless Pulse Oximetry
Intra-operative tissue oxygen monitoring: An unmet need

- Visual inspection is the only standard used today to assess tissue oxygenation ($\text{TiO}_2$)

- *Despite normal appearance*, compromised $\text{TiO}_2$ leads to life-threatening post-operative complications$^{1-4}$

4. Foppa C. *Tech in Coloproctology* 2014

8-20% of surgical anastomoses leak

**Esophageal cancer resection and stomach pull through**
The Costs of Anastomotic Leak

Patient Costs

• Secondary, corrective interventions required
• 10 - 30 additional days in hospital\(^1\)
• 3-fold increase in mortality rate\(^1\)
• 3-yr survival reduced to half\(^1\)

Economic Costs

• At MSKCC, $50K – 300K in additional costs from each esophagectomy leak

1. Rizk N. J AM Coll Surg 2004
**Wireless Pulse Oximeter (WiPOX)**

**Transmittance Oximetry**

There are no commercial tissue oximeters designed to work intra-operatively.

**Reflectance Oximetry**

- WiPOX utilizes reflectance oximetry technology
  - Allows application to internal organs
  - Measures pulsatile blood
  - Avoids confounding from venous congestion
Our Solution to the Unmet Need: WiPOX

The first tissue oximeter specifically designed for intra-operative use

- Optimized for: pH, temperature, presence of blood, contact force
- Pro-active surgeon involvement: measurement feedback for surgeon confidence
- Real-time display
- Wireless, hand-held,
- Procedure-specific, ergonomic design
Preclinical intraoperative testing of WiPOX

- WiPOX application to normal stomach & small bowel (rat and pig)
  - Normal tissue SpO₂ and pulse rate
- Mesenteric vessel occlusion
  - WiPOX detected bowel hypoxia with <30 seconds

SAGES 2011
Surg Endoscopy 2011 May
A Prospective Feasibility Study

- Following IRB approval, we tested our device on 12 patients
  - WiPOX detected compromised TiO₂ undetected by surgeons’ eye
  - No significant differences in serosal versus mucosal oxygenation

<table>
<thead>
<tr>
<th>Tissue oxygenation</th>
<th>TiO₂ (min-max)</th>
</tr>
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<tbody>
<tr>
<td>Before</td>
<td>88-99%</td>
</tr>
<tr>
<td>After</td>
<td>43-99%</td>
</tr>
</tbody>
</table>

Surgical forum 2011
J Am Coll Surg 2011

Four WiPOX test sites
A Blinded Prospective Clinical Trial Protocol

Esophageal or GEJ cancer undergoing esophagogastric resection/anastomosis

Exclusion Criteria:
- Reoperative Surgery
- Transhiatal esophagectomy
- Aborted procedure

Historical Controls (15% leak rate)

WiPOX determined TiO₂ at the site of planned anastomosis

Primary Endpoint:
Association between TiO₂ measurement & leak rate

Secondary Endpoint:
Association between TiO₂ measurement & stricture rate

WiPOX – Wireless Pulse Oximetry

Clinicaltrials.gov
NCT01551433
A Blinded Prospective Clinical Trial

Methods

- **Study period:** Jul 2012 - Jul 2014
- **n = 185** (2 benign disease, 1 GIST, rest for cancer)
- **Pre-operative therapy**
  - Induction chemoradiation 75%
  - Induction chemo 3%
- **Intra-operative assessment**
  - Measurement at the planned anastomotic site
  - Surgeon was blinded to the measurement
  - Surgical fellow performed the measurement and informed research study assistant
A Blinded Prospective Clinical Trial
Results

- Study participants = 114, non-participants = 69
- Among study participants (n = 114)
  - Gastric tissue oxygenation mean 90%, median 92% (range 62-100%)
  - Anastomotic leaks 8 (7%)
  - Anastomotic strictures 3 (2.6%)
  - Positive correlation between systemic and WiPOX-recorded heart rate (spearman rho=0.58, p<0.001)
  - No correlation between systemic pulse oximetry and WiPOX-recorded oxygenation (rho=0.08, p=0.4)
Systemic oxygenation does not reflect tissue oxygenation
A Blinded Prospective Clinical Trial
Results

Induction chemotherapy **does not** influence tissue oxygenation

Induction radiation therapy **does not** influence tissue oxygenation

\[ p = 0.421 \]

\[ p = 0.1 \]
A Blinded Prospective Clinical Trial

Results

<table>
<thead>
<tr>
<th></th>
<th>Study participants</th>
<th>Non-participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>114</td>
<td>69</td>
</tr>
<tr>
<td>Leaks</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Leak Rate</td>
<td>7%</td>
<td>12%</td>
</tr>
</tbody>
</table>

Anastomotic Leak Rate

Severity of Leaks

Grade IV 12%
Grade III 63%
Grade I 25%
Grade II 25%
Grade III 75%
Study Contributions – A positive study

<table>
<thead>
<tr>
<th>Surgeon’s Assumptions</th>
<th>Study data indicate</th>
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<tbody>
<tr>
<td>• Intraoperative tissue oxygenation determines anastomotic integrity</td>
<td>✗</td>
</tr>
<tr>
<td>• Systemic $O_2$ supplementation as a treatment</td>
<td>✗</td>
</tr>
<tr>
<td>• Gastric preconditioning as an option to decrease leak rates</td>
<td>✗</td>
</tr>
<tr>
<td>• Chemotherapy is the reason for anastomotic leaks</td>
<td>✗</td>
</tr>
<tr>
<td>• Radiation therapy is the reason for anastomotic leaks</td>
<td>✗</td>
</tr>
<tr>
<td>• Venous congestion may be the reason for anastomotic leaks</td>
<td>?</td>
</tr>
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</table>
### A Blinded Prospective Clinical Trial
**Strengths and Limitations**

#### Strengths
- Prospective single center study
- Multiple surgeon participation
- Uniform anastomotic technique
- Large cohort
- Comparable cohort of study non-participants
- Device designed specifically for esophagectomy with real-time display and real-time controls

#### Limitations
- Relative low anastomotic leak rates compared to historical control
  - Surgeon blinding not adequate
  - Hawthorne effect
- Continuous rather than single measurement may have been more informative
- Alterations in venous congestion may be as important as arterial perfusion
Thanks To CCNY-MSKCC Partnership Support

Manuscripts

Surgical Endoscopy
J Med Devices
J of Am Coll of Surgeons
(J Thor Cardvasc Surg)

U54 award acknowledged in 38 manuscripts to date

Patent
PCT/US2009/051424

Presentations

American Association for Thoracic Surgery
American College of Surgeons
Design of Medical Devices Conference
MDM East Conference
NYC Emerging Technologies Summit
NYC BioAccelerate
OneMed Conference
University Research & Entrepreneurship Symposium
World Congress of Endoscopic Surgery

WiPOX – Wireless Pulse Oximetry
## Wipox is Applicable to Critical Procedures With Preventable Complications

<table>
<thead>
<tr>
<th>Surgical Procedure</th>
<th>Complication Rate</th>
<th>Annual Procedures (US)</th>
</tr>
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<tbody>
<tr>
<td>GI anastomoses</td>
<td>15-20% (anastomotic leak)</td>
<td>300,000</td>
</tr>
<tr>
<td>CABG</td>
<td>8-10% (early graft closure)</td>
<td>450,000</td>
</tr>
<tr>
<td>Breast reconstruction surgery</td>
<td>15-20% (flap failure)</td>
<td>100,000</td>
</tr>
<tr>
<td>Solid organ transplantation</td>
<td>10%</td>
<td>100,000</td>
</tr>
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</table>

A reduction in complication rate of only 30% results in a savings of nearly $1B
WiPOX – A Multidisciplinary Multipurpose Project

Supported by U-54 Award

- Translating WiPOX
  - First prototype
    - Bioengineering students from the City College of New York
  - Optimization for the intraoperative use
    - In pigs
    - In humans
  - Pilot feasibility study in patients
  - Manufacturing and quality control
  - Clinical trial protocol & regulatory approvals
  - Patient enrollment
  - Trial completion

- Bioengineering Students Education & Training
- Surgical Resident Education & Training
- Clinical Research
- Device Commercialization
- Patient Care
Doctors Saved Lives, if Not Legs, in Boston

“What we like to do is before we take off someone’s leg — it’s extremely hard to make that decision — is we often get two surgeons to agree,” Dr. Tracey Dechert, a trauma surgeon at Boston Medical, said. “Am I right here? This can’t be saved. So that way you feel better and know that you didn’t take off someone’s leg that you didn’t have to take. All rooms had multiple surgeons so everyone could feel like we’re doing what we need to be doing.”
WiPOX First Generation

- Engineering verification
- Pre-clinical
- Clinical

Iterative design follows close collaboration of clinical and engineering teams.
WiPOX Second Generation

- Engineering verification
  (engineering design awards)

The City College of New York

Adaptive reticulating neck

“Quad-Balloon” contact correction and pressure sensing

Successful and complex biomedical engineering design with limited clinical utility
Experimental bridge system to test hypothesis supporting advanced multi-sensor systems
WiPOX Fourth Generation

Sensor net

Array of sensors

The City College of New York

Memorial Sloan Kettering Cancer Center
Thank You