A NONINVASIVE DEVICE FOR THE DETECTION AND MEASUREMENT OF INTRA-ABDOMINAL HEMORRHAGE

By

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UNIVERSITY OF FLORIDA

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To my family
ACKNOWLEDGMENTS

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# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACKNOWLEDGMENTS</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
<td></td>
<td>11</td>
</tr>
<tr>
<td>LIST OF ABBREVIATIONS</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td>CHAPTER</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>INTRODUCTION</td>
<td>18</td>
</tr>
<tr>
<td>Intra-abdominal Hemorrhage: Background and Significance</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>Diagnosing Intra-Abdominal Hemorrhage</td>
<td></td>
<td>18</td>
</tr>
<tr>
<td>Physical Examination</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Diagnostic Peritoneal Lavage</td>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Focused assessment with sonography for trauma (FAST)</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Computed tomography</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>Electrical Impedance Tomography</td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>Medical EIT</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td>Advantages of Medical EIT</td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Disadvantages of Medical EIT</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>Abdominal EIT</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>Hemiarray EIT</td>
<td></td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>ELECTRICAL BIOIMPEANCE THEORY AND METHODS</td>
<td>30</td>
</tr>
<tr>
<td>Four-Electrode Method</td>
<td></td>
<td>30</td>
</tr>
<tr>
<td>Electrode Contact Impedance</td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>Reciprocity</td>
<td></td>
<td>33</td>
</tr>
<tr>
<td>Drive Patterns</td>
<td></td>
<td>33</td>
</tr>
<tr>
<td>Adjacent drive</td>
<td></td>
<td>34</td>
</tr>
<tr>
<td>Opposite drive</td>
<td></td>
<td>34</td>
</tr>
<tr>
<td>Adaptive drive</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>Drive patterns for non-circular arrays</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>Hemiarray drive pattern</td>
<td></td>
<td>35</td>
</tr>
<tr>
<td>EIT Reconstruction</td>
<td></td>
<td>37</td>
</tr>
<tr>
<td>Difference Imaging</td>
<td></td>
<td>37</td>
</tr>
<tr>
<td>Laplace Equation</td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>Linearization of the EIT Reconstruction Problem</td>
<td></td>
<td>40</td>
</tr>
<tr>
<td>Lead Vector Theory</td>
<td></td>
<td>40</td>
</tr>
</tbody>
</table>
5 IN VIVO EXPERIMENTS

Electrodes .................................................................................................................. 89
Ingestion Model ......................................................................................................... 91
   Methods .................................................................................................................... 91
   Results ..................................................................................................................... 93
   Discussion .............................................................................................................. 98
Peritoneal Dialysis Model .......................................................................................... 98
   Methods ................................................................................................................... 99
   PD Reconstructions ............................................................................................... 102
   PD Quantification ................................................................................................. 104
      Static analysis ..................................................................................................... 106
      Dynamic analysis ................................................................................................ 106
   Discussion .............................................................................................................. 110

6 EPACK3 .................................................................................................................... 113

   Introduction .......................................................................................................... 113
   Analog System Redesign ....................................................................................... 113
      DDS Noise Reduction ......................................................................................... 115
      Current Source ................................................................................................... 119
         Input considerations ......................................................................................... 121
         Output compliance ........................................................................................... 121
         Noise ............................................................................................................... 122
         Output impedance ............................................................................................. 122
         Component selection ......................................................................................... 126
         Input capacitance compensation ....................................................................... 127
         Load compensation ........................................................................................... 127
         Lead-lag compensation ...................................................................................... 128
         Construction ....................................................................................................... 130
         Results and discussion ...................................................................................... 131
   Variable Gain Amplifier ......................................................................................... 134
   Digital System Redesign ......................................................................................... 135
      DSP ....................................................................................................................... 135
      Digital Clock Signals ............................................................................................ 136
      Power ................................................................................................................... 136
      Communications .................................................................................................. 136
      Printed Circuit Board and Construction ................................................................ 137
      DSP Code Design and Testing .............................................................................. 137
      Phase sensitive detector ....................................................................................... 138

7 SUMMARY AND CONCLUSIONS ........................................................................... 142

APPENDIX

PROCEDURE FOR MAKING TX-151 BLOOD EQUIVALENT ANOMALY .................... 145
LIST OF REFERENCES ............................................................................................................................................... 146

BIOGRAPHICAL SKETCH ......................................................................................................................................... 156
<table>
<thead>
<tr>
<th>Table</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1</td>
<td>25</td>
</tr>
<tr>
<td>5-1</td>
<td>91</td>
</tr>
<tr>
<td>5-2</td>
<td>106</td>
</tr>
<tr>
<td>5-3</td>
<td>110</td>
</tr>
<tr>
<td>A-1</td>
<td>145</td>
</tr>
</tbody>
</table>

**Table 1-1**  
Electrical properties of biomaterials relevant to the detection of IAH

**Table 5-1**  
Comparison of TENS electrodes

**Table 5-2**  
Quantification of dialysate mass in two patients.

**Table 5-3**  
Confusion matrix for detection of modeled IAH using a threshold of 60 mL/min.

**Table A-1**  
Composition of blood equivalent anomaly
<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1</td>
<td>Transverse section through the abdomen</td>
<td>21</td>
</tr>
<tr>
<td>1-2</td>
<td>FAST image showing unidentified free fluid in Morrison’s pouch</td>
<td>22</td>
</tr>
<tr>
<td>1-3</td>
<td>Comparison of the locations of the electrodes</td>
<td>28</td>
</tr>
<tr>
<td>2-1</td>
<td>Illustration of the measurement of transfer impedance of an arbitrary volume conductor</td>
<td>30</td>
</tr>
<tr>
<td>2-2</td>
<td>Comparison of the effect of electrode contact impedance</td>
<td>32</td>
</tr>
<tr>
<td>2-3</td>
<td>Illustration of the Reciprocity Theorem</td>
<td>34</td>
</tr>
<tr>
<td>2-4</td>
<td>Measurement of the 40 transimpedances in the hemiarray drive pattern</td>
<td>36</td>
</tr>
<tr>
<td>2-5</td>
<td>Sequence of transimpedance measurements using the hemiarray electrode configuration</td>
<td>36</td>
</tr>
<tr>
<td>2-6</td>
<td>Illustration of the Compensation Theorem</td>
<td>41</td>
</tr>
<tr>
<td>2-7</td>
<td>Two dimensional forward problem model and mesh</td>
<td>43</td>
</tr>
<tr>
<td>2-8</td>
<td>Two dimensional forward problem solutions showing the lead field vector for each port in the hemiarray</td>
<td>44</td>
</tr>
<tr>
<td>2-9</td>
<td>Average spatial sensitivity to impedance change</td>
<td>45</td>
</tr>
<tr>
<td>2-10</td>
<td>Synthetic l-curve</td>
<td>48</td>
</tr>
<tr>
<td>3-1</td>
<td>EPack1 System Diagram</td>
<td>55</td>
</tr>
<tr>
<td>3-2</td>
<td>EPack2 System Diagram</td>
<td>58</td>
</tr>
<tr>
<td>3-3</td>
<td>Schematic of Bipolar Howland Current Source with Negative Impedance Converters</td>
<td>60</td>
</tr>
<tr>
<td>3-4</td>
<td>Photograph of Bipolar Howland Current Source with Negative Impedance Converters</td>
<td>61</td>
</tr>
<tr>
<td>3-5</td>
<td>Functional schematic of Analog Devices ADG408 8-1 analog multiplexer</td>
<td>62</td>
</tr>
<tr>
<td>3-6</td>
<td>Functional schematic of Intersil CD22M3494 16-8 analog crosspoint switch</td>
<td>64</td>
</tr>
<tr>
<td>3-7</td>
<td>Schematic of the bootstrapped AC follower voltage preamplifier</td>
<td>67</td>
</tr>
<tr>
<td>3-8</td>
<td>List of EPack2 commands</td>
<td>72</td>
</tr>
<tr>
<td>Page</td>
<td>Image/Content</td>
<td></td>
</tr>
<tr>
<td>------</td>
<td>---------------</td>
<td></td>
</tr>
<tr>
<td>3-9</td>
<td>Comparison of the EPack1 and EPack2 data packets.</td>
<td></td>
</tr>
<tr>
<td>3-10</td>
<td>Screenshot of the EPack Control Center GUI.</td>
<td></td>
</tr>
<tr>
<td>3-11</td>
<td>EPack1 PCB.</td>
<td></td>
</tr>
<tr>
<td>3-12</td>
<td>EPack1 enclosure.</td>
<td></td>
</tr>
<tr>
<td>3-13</td>
<td>EPack2 enclosure.</td>
<td></td>
</tr>
<tr>
<td>4-1</td>
<td>Schematic of resistor phantom.</td>
<td></td>
</tr>
<tr>
<td>4-2</td>
<td>Photograph of the cylindrical saline phantom.</td>
<td></td>
</tr>
<tr>
<td>4-3</td>
<td>Experimental setup for measuring the spatial variability of QI.</td>
<td></td>
</tr>
<tr>
<td>4-4</td>
<td>Experimental setup for measuring the longitudinal variability of QI.</td>
<td></td>
</tr>
<tr>
<td>4-5</td>
<td>Comparison of the variability of the QI.</td>
<td></td>
</tr>
<tr>
<td>4-6</td>
<td>Aperture time comparison.</td>
<td></td>
</tr>
<tr>
<td>4-7</td>
<td>Comparison of the SNR on measurements of the resistor phantom using EPack 1 and EPack2.</td>
<td></td>
</tr>
<tr>
<td>4-8</td>
<td>Signal and noise in the resistor phantom measured by EPack2.</td>
<td></td>
</tr>
<tr>
<td>5-1</td>
<td>Photograph of five candidate TENS electrodes.</td>
<td></td>
</tr>
<tr>
<td>5-2</td>
<td>Electrodes in hemiarray configuration.</td>
<td></td>
</tr>
<tr>
<td>5-3</td>
<td>Time plots of each transimpedance against time in the soup model.</td>
<td></td>
</tr>
<tr>
<td>5-4</td>
<td>Comparison of the SNR measured using the EPack2 in different targets.</td>
<td></td>
</tr>
<tr>
<td>5-5</td>
<td>$l$-curve for an EIT measurement taken after a subject ingested soup.</td>
<td></td>
</tr>
<tr>
<td>5-6</td>
<td>Comparison of QI calculated using different regularization parameters, $k$.</td>
<td></td>
</tr>
<tr>
<td>5-7</td>
<td>Images, mass estimate and mass flow rate estimate measured during ingestion of soup.</td>
<td></td>
</tr>
<tr>
<td>5-8</td>
<td>Breathing artifact in QI in ingestion model.</td>
<td></td>
</tr>
<tr>
<td>5-9</td>
<td>Illustration of peritoneal dialysis.</td>
<td></td>
</tr>
<tr>
<td>5-10</td>
<td>Measuring the mass of the dialysate.</td>
<td></td>
</tr>
<tr>
<td>5-11</td>
<td>Time series of a single EIT session.</td>
<td></td>
</tr>
</tbody>
</table>
Regression analysis of the QI-mass relationship for nine data sets..........................104
Results monitoring impedance changes in IAH model over time. ..............................105
Distribution of estimated mass flow rates in positive and negative models of IAH........108
ROC curve for the detection of IAH........................................................................109
EPack3 system overview .........................................................................................114
DDS output spectrum...............................................................................................115
Bandpass filter for preconditioning the voltage reference to the current source. .........117
Bandpass filter transfer function..............................................................................118
Bandpass filter output referred noise.................................................................119
Improved Howland current source........................................................................120
Linear model of the improved Howland current source................................................120
Compensating for parasitic input capacitance at the inverting opamp input using a feedback capacitance. ..................................................................................128
Lead-lag compensated, improved Howland current source..........................................129
EPack3 analog subsystem PCB. ...............................................................................130
Loop gain plot of compensated and uncompensated Howland current sources using the OPA847 opamp ..............................................................................131
Output impedance of lead-lag compensated, improved Howland current source.........132
Frequency content of the PSD................................................................................139
Flowchart of the PSD algorithm..............................................................................140
Electrode array for the detection of intra-ventricular hemorrhage..............................143
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAT</td>
<td>Blunt abdominal trauma</td>
</tr>
<tr>
<td>CCS</td>
<td>Constant current source</td>
</tr>
<tr>
<td>CCVS</td>
<td>Current controlled voltage source</td>
</tr>
<tr>
<td>CEUS</td>
<td>Contrast enhanced ultrasound</td>
</tr>
<tr>
<td>CMFB</td>
<td>Common-mode feedback</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>DAS</td>
<td>Data acquisition system</td>
</tr>
<tr>
<td>DC</td>
<td>Direct current</td>
</tr>
<tr>
<td>DDS</td>
<td>Direct digital synthesis; or, direct digital synthesizer</td>
</tr>
<tr>
<td>DIP</td>
<td>Dual inline package</td>
</tr>
<tr>
<td>DPL</td>
<td>Diagnostic peritoneal lavage</td>
</tr>
<tr>
<td>DSP</td>
<td>Digital signal processor</td>
</tr>
<tr>
<td>EIT</td>
<td>Electrical impedance tomography</td>
</tr>
<tr>
<td>EMI</td>
<td>Electromagnetic interference</td>
</tr>
<tr>
<td>FAST</td>
<td>Focused assessment with sonography in trauma</td>
</tr>
<tr>
<td>FEM</td>
<td>Finite element method</td>
</tr>
<tr>
<td>FIFO</td>
<td>First in, first out buffer</td>
</tr>
<tr>
<td>$f_0$</td>
<td>Operating frequency of the current source</td>
</tr>
<tr>
<td>FPR</td>
<td>False-positive rate</td>
</tr>
<tr>
<td>IAH</td>
<td>Intra-abdominal hemorrhage</td>
</tr>
<tr>
<td>IC</td>
<td>Integrated circuit</td>
</tr>
<tr>
<td>In-amp</td>
<td>Instrumentation amplifier</td>
</tr>
<tr>
<td>LPF</td>
<td>Low pass filter</td>
</tr>
<tr>
<td>$n_c$</td>
<td>Number of averaged cycles in a transimpedance measurement</td>
</tr>
</tbody>
</table>
\( n_E \) Number of electrodes in an EIT system
\( n_M \) Number of transimpedances in an EIT measurement frame; the length of the vector \( \Delta Z_M \)
\( n_P \) Number of pixels in the EIT reconstruction
Op-amp Operational amplifier
PC Personal computer
PCB Printed circuit board
PLCC Plastic leadless chip carrier
PD Peritoneal dialysis
PSD Phase sensitive detection
PWM Pulse width modulation
RMS Root mean square
ROC Receiver operator characteristic
SCI Serial communication interface
SEM Standard error of measurement
SVD Singular value decomposition
SNR Signal-to-noise ratio, usually specified in decibels (dB)
TENS Transcutaneous electrical neural stimulation
TPR True-positive rate
TSVD Truncated singular value decomposition
UART Universal asynchronous receiver/transmitter
US Ultrasound
USB Universal serial bus
WMN Weighted minimum norm
QI Quantity index, the integral of pixels in an EIT reconstruction
<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>( Z_E )</td>
<td>Electrode contact impedance</td>
</tr>
<tr>
<td>( Z_M )</td>
<td>Mutual transfer impedance</td>
</tr>
</tbody>
</table>
Abstract of Dissertation Presented to the Graduate School of the University of Florida in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy

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By

Aaron Scott Tucker

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Chair: Rosalind J. Sadleir
Major: Biomedical Engineering

Bomb blasts, motor vehicle collisions, and falls can cause intra-abdominal hemorrhage (IAH), a potentially life-threatening condition. Electrical impedance tomography (EIT) using electrodes placed sole on the anterior abdomen was proposed as a method for the detection and quantification of IAH. EIT devices and methodology were developed and tested in models of IAH. The EPack, a prototype EIT device, was designed to collect data to verify the method. The small footprint device was optimized to rapidly identify IAH with little operator input. The device was tested in resistive and saline-tank phantoms. The newest generation device has significantly improved performance in terms of speed and accuracy compared to its predecessor, despite its slimmer profile. Two in vivo models were used to assess the EPack’s ability to detect active IAH. In one model, a volunteer drink chicken soup with the same conductivity as accumulating blood. In the second model, peritoneal dialysis were monitored during a routine dialysate exchange. In both models, the volume of conductive fluid introduced into the abdomen was detected using the EPack. Results showed strong sensitivity to both ingested and injected conductive fluids, and suggest that hemorrhage rates greater than 60 ml/min can be detected with 98% sensitivity and 95% specificity.
CHAPTER 1
INTRODUCTION

Intra-abdominal Hemorrhage: Background and Significance

The abdomen is the region of the body located between the diaphragm and the pelvis. The abdominal contents are divided by the peritoneum. Intraperitoneal abdominal contents include the stomach, spleen, liver and intestines. Retroperitoneal structures include the bladder, pancreas, spleen, kidneys, inferior vena cava and aorta.

These vital organs, and the vasculature perfusing them, are vulnerable to brute forces associated with motor vehicle accidents, falls, battlefield explosions and other blunt traumas because they are not protected by bone. More than four in five fatal traumatic abdominal injuries are caused by blunt abdominal trauma (BAT) (Rozycki et al. 1993). Gedeborg et al. reported that the undiagnosed injuries having the greatest impact on survival rates were damaged abdominal and pelvic organs (2009).

Intra-abdominal hemorrhage (IAH) secondary to BAT can lead to hypovolemic shock, ischemia and death when blood loss approaches 40% of total blood volume, about one liter of blood (Dutton 2002). The most common causes of IAH as a consequence of BAT are lacerations to the splenic, hepatic, and gastrointestinal vasculature (Yao et al. 2002; Ozturk et al. 2004).

Diagnosing Intra-Abdominal Hemorrhage

Rapid detection of moderate to severe IAH significantly improves outcomes (Garrison et al. 1996), but IAH is hard to diagnose because the damage is hidden. Severe IAH must receive prompt exploratory laparotomy, hemostasis and infusions. One study of the relationship between the time to laparotomy in IAH victims and survival rates in 243 patients found that the mortality rate increased about 1% for each 3 minutes of delay (Clarke et al. 2002).
Because of the acute potential for fatality due to rapid hemorrhage, the speed of the diagnosis is equally important to the quality (sensitivity and specificity) of the detection method.

A goal secondary to detection of IAH is determining its severity. The rate of hemorrhage is an indicator of the extent of internal trauma. Patients with mild bleeding benefit from nonoperative management (Goan, Huang and Lin 1998), therefore determining the hemorrhage rate can prevent unnecessarily invasive interventions.

**Physical Examination**

Clinical signs of hypovolemia include hemodynamic instability (hypotension, low hematocrit), pallor, clammy skin, decreased urinary output and anxiety. Physiological indicators of abdominal injuries can be misleading, inconclusive, unreliable, nonspecific, or may not manifest until the patient is already at significant risk. Notably, young individuals can withstand losing as much as 45% of their blood volume before losing blood pressure (Gaines 2009). Diagnoses based exclusively on physical examination have sensitivity of 60% at best (Lowe *et al.* 1972). Diagnosis by physical examination is further complicated by the fact that roughly a quarter of trauma patients’ mental state is compromised by concurrent head trauma or intoxication (Wilson, Schwarccz and Pilcher 1965).

**Diagnostic Peritoneal Lavage**

Diagnostic peritoneal lavage (DPL) is an invasive procedure to detect hemoperitoneum that has been used for over half a century (Root *et al.* 1965). Isotonic saline solution is percutaneously injected into the abdomen via a catheter, and after a short dwell period, siphoned out and visually inspected for blood. The concentration of red blood cells (RBC) in the retrieved saline is indicative of the severity of the bleeding (Feied 1989).

DPL has high sensitivity for internal bleeding, however the invasive procedure has a complication rate as high as 5% (Soderstrom, DuPriest and Cowley 1980; Thomas *et al.* 1997).
DPL gives only a vague sense of the severity of bleeding, relies on clinical interpretation, doesn’t diagnose retroperitoneal hemorrhage, and can sometimes give false results when bleeding is caused by the placement of the DPL catheter (Henneman 1990). DPL has fallen out of favor over the last two decades because of its invasiveness, in favor of newer imaging modalities.

**Imaging**

Imaging modalities conventionally used to diagnose IAH are sonography (Rozycki et al. 1993) and computed tomography (CT) (Stafford et al. 1999). The former is rapid and somewhat portable and the latter has high sensitivity and specificity. However, neither is suited for continuous monitoring or measuring haemorrhage rate, and the accuracy of both methods depends on a technician well-trained in device operation and image interpretation.

Morison’s pouch (the hepatorenal recess) is the lowest point in the supine abdomen and therefore tends to collect free blood. Figure 1-1 shows a cross-section of the abdomen highlighting Morison’s pouch. Other potential spaces where blood can accumulate are the left and right subphrenic spaces, right subhepatic space, left perisplenic area, and the pelvis (McKenney et al. 2001). These spaces define the regions of interest for bioimaging diagnosis.

**Focused assessment with sonography for trauma (FAST)**

Ultra sonography (US) is the newest modality for detecting internal bleeding. US uses reflected high frequency acoustic waves to image internal anatomical structures. Focused Assessment with Sonography for Trauma (FAST) is a US protocol that has been widely adopted, and that has widely replaced DPL. The FAST protocol examines four areas for free fluid: the pericardium; the perihepatic region and hepato-renal recess; the perisplenic and left-perirenal space; and the pelvis and perivesical area.

In most trauma centers, US is used to make the primary diagnosis for IAH. If indicated by US results or patient history, CT will be used to as a secondary diagnosis (Scaglione 2004).
Advantages of US include portability, lack of ionizing radiation and invasiveness, low cost, and speed of diagnosis. A typical FAST examination is reported to take less than seven minutes on average (McKenney et al. 1996). US equipment is more available due to its smaller size and lower cost (Arrillaga et al. 1999); however, not all US equipment is suitable for FAST examinations (Blaivas and Theodoro 2002).

Sensitivity to intra-abdominal hemorrhage using FAST has been reported to be as low as 79% (Catalano et al. 2009) or as high as 98% (Branney et al. 1997). In cadavers, US has been
used to detect as little as 100mL of free fluid (Goldberg et al. 1973). But sensitivity to hemoperitoneum resulting from pelvic fracture has been reported to be low (Friese et al. 2007).

Contrast enhanced ultrasound (CEUS) can be used to better localize the bleeding site, at the expense of additional time and patient discomfort (Liu et al. 2002, Catalano et al. 2009). CEUS has been reported to be almost as sensitive as CT to solid organ injury (Catalano et al. 2009).
Despite the advantages of FAST, the technique can be challenging to use. FAST requires a trained operator whose interpretation can be subjective (Boulanger et al. 1998; Shackford et al. 1999; Sirlin et al. 2004). The subjectivity of the FAST examination is highlighted by Figure 1-2. Furthermore, ultrasound is unable to measure the volume of free blood or the bleeding rate. And although FAST is repeatable, it cannot be used for continuous monitoring.

**Computed tomography**

Computed tomography (CT) is a radiological technique that uses x-rays to obtain three-dimensional images of a subject. CT can detect as little as 30mL of accumulating blood, and can sometimes identify the source of the hemorrhage (Federle et al. 1981). CT is useful for detecting retroperitoneal bleeds that cannot be evaluated using US, and for determining the severity of injuries indentified with FAST in stable patients (Dolich et al. 2001).

CT is currently the gold standard in IAH detection, but the size and expense of CT equipment limits its usefulness. Because CT scanners are not portable, patients with suspected trauma must be transported to the scanner. This is impractical in many hospitals if the patient is unstable (Dolich et al. 2001). A CT scan takes around fifteen minutes, during which the patient cannot undergo further diagnoses or treatments. Limited availability of the CT scanner in many institutions can further slow the diagnosis. Although CT is noninvasive, it does expose patients (and operators) to radiation. Radiographic oral contrast material may also be used to increase sensitivity to blood, although its necessity has been questioned (Stafford et al. 1999). Like US, CT is unable to diagnose the rate of hemorrhage (Yao et al. 2002).

**Electrical Impedance Tomography**

Electrical Impedance Tomography (EIT) is an emerging imaging technique used to map the spatial distribution of electrical conductivity within an object. EIT can distinguish the space occupied by materials based on their characteristic electrical conductivity. It is possible to
observe changes in those materials over time by collecting a sequence of measurements. In medical applications, dynamic impedance changes measured using EIT can be used to determine the rate of processes in the body.

EIT was originally developed for geological studies (Stephanesco and Schlumberger 1930), and has been used to detect cracks (Alessandrini and Rondi 1998), air bubbles (Ljaz et al. 2008), groundwater (Nobes 1996), landmines (Wort et al. 1999), and corrosion (Vilhunen et al. 2002).

EIT methods vary appropriate to the application, but generally involve the following steps. First, an electrode array is placed around the boundary of a volume conductor. A carefully calibrated electrical current is injected into the volume conductor using some of the electrodes. The electrical potential distribution created by the current depends on the conductivity distribution within the volume conductor. The remaining electrodes are used to measure the electrical potential at the surface.

This process is repeated in succession, using different sets of electrodes to apply the electric current and sense the boundary voltage until the maximal number of independent measurements is made. The measured boundary voltages can then be used, in conjunction with a priori assumptions, to determine the impedance distribution within the region of interest.

**Medical EIT**

EIT has been used to image the head (Tang 2010; Romsauerova et al. 2006), heart (Dazzani et al. 2005), lungs (Adler et al. 1997; Frerichs 2000; Zlochiver et al. 2007), and stomach (Mangnall et al. 1991; Nour et al. 1995). EIT has been proposed for detecting cancers of the breast (Soni et al. 2004; Tizzard et al. 2010) and the prostate (Halter et al. 2007). EIT can
Table 1-1. Electrical properties of biomaterials relevant to the detection of IAH

<table>
<thead>
<tr>
<th>Material</th>
<th>Resistivity (Ωm)</th>
<th>Conductivity (S/m)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>1.4</td>
<td>0.7</td>
<td>Shimazu et al. 1981</td>
</tr>
<tr>
<td>Peritoneal Dialysate</td>
<td>0.8</td>
<td>1.2</td>
<td>Tucker et al. 2010</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.9</td>
<td>0.53</td>
<td>Carrara 2010</td>
</tr>
<tr>
<td>Liver</td>
<td>14.3</td>
<td>0.07</td>
<td>Gabriel et al 1996</td>
</tr>
<tr>
<td>Spleen</td>
<td>8.3</td>
<td>0.12</td>
<td>Gabriel et al 1996</td>
</tr>
<tr>
<td>Abdominal Bulk Average</td>
<td>5.0</td>
<td>0.2</td>
<td>Barber and Brown 1984</td>
</tr>
</tbody>
</table>

also be used to measure blood flow (Vonk-Noordegraaff et al. 1997) and body temperature (Conway 1987; Moskowitz et al. 1995).

The electrical impedance of biological tissues is well documented. Carrara maintains an exceptionally detailed database that is available online (2010). Pathological tissues also have characteristic conductivities (Shini and Rubinsky 2007; Keshtkar and Keshtkar 2007). Table 1-1 shows a list of impedances relevant in the detection of IAH.

Free blood has a resistivity of about 1.5 Ωm (Shimazu et al. 1981) compared with the average resistivity of the abdominal tissues of 5 Ωm (Barber and Brown 1984). This study exploited this high conductivity contrast to detect and quantify IAH.

**Advantages of Medical EIT**

EIT has potential advantages compared to other diagnostic techniques for detecting IAH. EIT is safe. It is noninvasive, does not require handling of biological fluids, and does not expose the patient (or the operator) to ionizing radiation.

EIT can be rapidly deployed. It has low barriers to implementation due to its low cost and because it is easy to use. EIT is better suited for continuous monitoring than CT or US. The EIT system operates autonomously without need for an operator once the electrodes are placed on the patient. EIT is complimentary to existing technology for bleeding detection. It can be used in conjunction with US and CT to provide early detection of IAH.
Disadvantages of Medical EIT

The spatial resolution of EIT reconstructions is inherently limited because the wavelength used in typical EIT is several thousand meters long. The EIT reconstruction is also highly sensitive to electrical interference, electrode placement error, and errors in the assumed boundary shape. Small measurement imprecision from these error sources can cause significant artifacts in the reconstructed image due to the ill-posed nature of the EIT reconstruction.

It is unlikely that high-resolution, low noise images comparable to modern CT images will ever be obtained using this form of EIT. Rather than endeavor to improve the image quality, we have proposed a method to extract parametric information from the image that can quantify impedance changes with respect to time.

Abdominal EIT

In the 1990s, Sadleir and Fox began groundbreaking work using EIT to detect IAH. Their research focused on quantitative estimators of bleeding in the abdomen inspired by similar studies of gastric emptying (Mangnall et al. 1987), and pulmonary plethysmography (Adler et al. 1997). They proposed a parameter that was proportional to the volume of a resistive anomaly, called the quantity index (QI). QI was tested in a series of experiments using instrumentation based on the classic Sheffield Mark I (Brown and Seagar 1987), and with sixteen electrodes equidistantly spaced in a ring around the abdomen.

Two important results were obtained (Sadleir and Fox 1998). First, QI was shown to be a better estimator of volume than other candidate parameters. Second, QI was shown to be spatially variable. Anomalies appeared to grow as they moved from the center of the phantom towards its boundary, and appeared to shrink as they moved longitudinally away from the electrode plane.
Spatial variability is an undesirable quality in the QI, especially if the anomaly location is not known *a priori*. In a similar set of experiments, they found that by using elongated bar electrodes instead of point electrodes, the longitudinal sensitivity was significantly improved. Through characterization of the radial dependence, a correction filter was designed to compensate radial volume variation.

The selectivity of QI was also explored in the study. The contribution of interfering phenomena, including digestion, breathing, and motion artifacts, was examined and found to be significant (Sadleir and Fox 2001).

An abdominal electrode belt was designed to affix electrodes more rapidly and accurately than was possible using individual discrete electrodes (Sadleir, Fox and Turner 2000). The belt inflated to provide good electrode contact in different sized people.

A pilot study was conducted to determine if QI could quantify conductive fluid in an *in vivo* IAH model (Sadleir and Fox 2001). Peritoneal dialysis (PD), an invasive procedure used to clear waste in patients with renal failure, was identified as an appropriate model for IAH. EIT was expected to have a strong sensitivity to peritoneal dialysate because it has twice the conductivity of blood. Bleeding rates exceeding 100 mL/min were reliably detectable and measurable using the QI. The authors found less variation from individual to individual than was expected.

Additional evidence that EIT can detect IAH was collected in a pig model (Wanjun et al. 2008). In the study, hemorrhage was modeled by injecting anticoagulated blood into five anesthetized pigs while undergoing EIT monitoring. Their findings were essentially identical to those of Sadleir and Fox.
Hemiarray EIT

IAH is often accompanied by other traumatic injuries that can be exacerbated by unnecessary movement. The inflatable belt proved efficient and convenient for models of bleeding, but it is not possible to apply the belt without moving a supine patient. Placing electrodes around the abdomen of a trauma victim without first evaluating concurrent injuries is risky. Designing an EIT methodology that does not require moving a supine patient was a major challenge.

This study introduces an abdominal EIT method that doesn’t require moving a supine patient. To avoid aggravating existing injuries, electrodes were applied only to the anterior abdomen – anatomy readily accessible on a supine patient. A schematic of the *hemiarray* electrode arrangement is shown in Figure 1-3. Limiting electrodes to the anterior abdomen

![Figure 1-3. Comparison of the locations of the electrodes in the (a) full and (b) hemi abdominal arrays.](image)
reduces the risk of complicating undiagnosed injuries, but without electrodes on the posterior abdomen the resolution, sensitivity, and localization accuracy of EIT are reduced.

This dissertation describes the use of the hemiarray electrode configuration to detect and quantify IAH. While EIT has traditionally focused on reconstructing tomographic images of the impedance change, in this study EIT was used to obtain quantitative estimators useful for the detection of IAH. In the Chapter 2, the reconstruction theory and methods used for quantitative EIT are introduced and discussed. Chapter 3 describes the requirements and design of an EIT data acquisition system (DAS) compatible with the hemiarray configuration. Chapter 4 details phantom experiments designed to test and optimize the reconstruction methods, and the performance of the DAS. Experiments using the DAS and hemiarray reconstruction methods in two in vivo models of IAH are detailed in Chapter 5. Based on the results from phantom and in vivo experiments, modifications in the DAS are described in Chapter 6. Finally, Chapter 7 discusses the implications of this study’s results, and proposes improvements and directions for future studies.
CHAPTER 2
ELECTRICAL BIOIMPEDANCE THEORY AND METHODS

This chapter discusses the bioelectrical theory and methods that were used for EIT detection of IAH. The EIT measurand is the change in electrical transfer impedance, $\Delta Z_M$. This quantity is related to internal conductivity changes by the forward and inverse reconstruction problems. Solutions of the reconstruction problems are discussed, leading to a linear algorithm for quantifying the amount and accumulation rate of abdominal blood.

**Four-Electrode Method**

EIT measures the transfer impedance, $Z_M$, of a two-port electrical network (Grimnes and Martinsen 2000). For any two-port network, transfer impedance (or transimpedance) is the current-to-voltage gain from one port to another. Measuring $Z_M$ requires four electrodes, as illustrated in Figure 2-1. Electrodes $A$, $B$, $C$ and $D$ are placed along the boundary of the volume conductor, $\Omega$. A pair of electrodes defines a port; electrode pairs $\{A, B\}$ and $\{C, D\}$ form ports $\Phi$ and $\Psi$, respectively.

![Figure 2-1. Illustration of the measurement of transfer impedance of an arbitrary volume conductor.](image-url)
Each port has a differential voltage, $V$, and differential current, $I$. Transfer impedance is defined as the ratio

$$Z_M \triangleq \left. \frac{V}{I} \right|_{I_v=0}$$

(2-1)

where $I_\Phi$ is the current flowing in port $\Phi$ that causes an open-circuit voltage $V_\Psi$ to develop at port $\Psi$ (Alexander and Sadiku 2004).

$Z_M$ is frequency dependent and can be expressed as a complex number:

$$Z_M(\omega) = R(\omega) + jX(\omega)$$

(2-2)

where $R(\omega)$ and $X(\omega)$ are respectively the frequency-dependent resistive and reactive components of $Z_M$, and $\omega$ is the angular frequency. Transfer impedance is a function of the conductivity, $\sigma$, permittivity, $\varepsilon$, the geometry of the domain, and the selection of ports.

**Electrode Contact Impedance**

Four-electrode impedance measurements were made in preference to the simpler two-electrode method because of the effect of the electrode-skin contact impedance, $Z_E$. The contact impedance is a theoretical construct that accounts for the energy lost at the electrode-electrolyte interface, the boundary between the metallic conductors in the electronic circuitry and the ionic conductors within the human body. The contact impedance is a function of many variables, including the material composition and geometry of the electrode, the ambient temperature, the pressure exerted on the electrode, and the ionic concentration and availability within the skin (Grimnes 1983). Depending on these factors the electrode impedance can range from tens of ohms to hundreds of kilohms.

Due to the many variables that affect it, the contact impedance in most bioimpedance techniques is unknown and varying with time. When $Z_E$ is unknown the transimpedance cannot
be measured using a two-electrode method. This is illustrated in Figure 2-2A. The applied current flows through the series combination of two electrode impedances, $Z_{E1}$ and $Z_{E2}$, plus the transimpedance, $Z_M$. The resulting voltage, measured as the difference between the potentials at each electrode, is the product of the applied current and the series combination of the three impedances. Therefore the two electrode method will measure a total impedance of $Z_{E1} + Z_M + Z_{E2}$, and, unless the contact impedances are known, $Z_M$ cannot be determined. Worse, if $Z_{E1}$ and $Z_{E2}$ are much larger than $Z_M$, then $Z_M$ may be obscured beyond the accuracy or precision of the measurement system.

![Diagram of two-electrode and four-electrode impedance measurements]

Figure 2-2. Comparison of the effect of electrode contact impedance in A) two-electrode and B) four-electrode impedance measurements.
The four-electrode method solves this problem by separating the injection of current and the sensing of the potential, as shown in Figure 2-2B. The current still travels through the series combination of $Z_{E1}, Z_{E2},$ and $Z_M,$ but now the voltage is measured only across $Z_M$ through the addition of two electrodes. This is because the contact impedances of the additional electrodes, $Z_{E3}$ and $Z_{E4},$ are negligible to the high input impedance of the voltmeter. Because no current flows through $Z_{E3}$ and $Z_{E4},$ there is no voltage drop across them. Thus, the voltage difference across the voltmeter terminals is the same as the voltage difference across $Z_M.$

**Reciprocity**

According to Helmholtz’s reciprocity theory, when a four-electrode (two-port) measurement is made on a linear network with no internal sources, the measured transfer impedance will be the same if the injection and sensing ports are interchanged (1853). According to the reciprocity theory, if current $I_\psi$ is injected in port $\Phi$ and the voltage $V_\psi$ is measured from port $\Psi,$ or if current $I_\psi$ is injected in port $\Psi$ and the voltage $V_\phi$ is measured from port $\Phi,$ the same transimpedance is measured:

$$Z_M = \frac{V_\psi}{I_\psi} \bigg|_{I_\psi \neq 0} = \frac{V_\phi}{I_\psi} \bigg|_{I_\psi \neq 0}$$  \hspace{1cm} (2-3)

This important, and sometimes surprising, relationship is illustrated in Figure 2-3.

**Drive Patterns**

An EIT measurement frame is composed of a series of transimpedance measurements made using a multiplicity of electrodes placed around the boundary of interest. The total number of transfer impedances that are measured, $n_M,$ depends on the number of electrodes and the current injection pattern. Each EIT measurement frame is represented by a measurement vector, $Z_M,$ whose length is $n_M.$
The drive pattern refers to the combinations of electrodes chosen to transmit current. Some of the most common drive patterns for abdominal EIT are highlighted below. Each pattern assumes the electrodes are equidistantly spaced in a ring around the abdomen.

**Adjacent drive**

The adjacent pattern injects current through nearest neighbor electrodes. In the adjacent pattern, the current source and sink are always next to each other (Malmivuo and Plonsey 1995). This pattern is best for resolving small objects (Schuessler and Bates 1998), and has the most independent measurements for a given number of electrodes.

**Opposite drive**

The opposite pattern uses pairs of electrodes on opposite sides of the boundary to inject current, and is perhaps the most intuitive of the drive patterns. The opposite current pattern has been shown to have better sensitivity in the center of the body (Cheney and Isaacson 1992), but it yields fewer independent measurements for a given number of electrodes.
Adaptive drive

The adaptive pattern is a relatively newer technique that injects current into each electrode simultaneously. Using the adaptive pattern, there are more than two electrodes simultaneously used for current injection. The amplitude of the current at each electrode is modulated to approximate a rotating, uniform electric field (Gisser et al. 1988). In these systems, the current sources must be vigilantly calibrated. Imperfections in the matching of each source will contribute to common mode error.

Drive patterns for non-circular arrays

Patterns for non-circular electrode arrays also been used in medical EIT. Some interesting examples include a rectangular grid for thoracic EIT (Mueller et al. 2001) and an EEG-based layout for brain imaging (Tang 2008).

Hemiarray drive pattern

The hemiarray is a unique electrode array proposed for detection IAH. The advantage of this layout is that it can be applied without moving the patient. By only applying electrodes to the anterior abdomen, the hemiarray reduces the risk of complicating injuries consequent to blunt trauma; however, the sensitivity to the posterior abdomen is somewhat reduced.

The adjacent and opposite measurement patterns used in other EIT systems were combined and adapted for use with the hemiarray. The hemiarray drive pattern is a hybrid of the adjacent and opposite patterns that maximizes the number of independently measurable transimpedances. Simply explained, the hemiarray pattern is an adjacent pattern that considers the first and last electrodes as if they were adjacent, although they are actually an opposite pair. Currents and voltages ports are defined using this definition of “adjacent” electrodes.

Using the hemiarray pattern with $n_E$ electrodes there are $n_E$ current drive pairs. For a given current pair, differential voltages are measured between pairs of adjacent electrodes, neglecting
electrodes selected for current transmission. \((n_E - 3)\) differential voltages are sequentially measured in this fashion before the injection pair is changed. In total, \(n_E(n_E - 3)\) voltages are measured, half of which are independent measurements due to reciprocity.

The measurements are taken in a standard order that progresses from the first electrode towards the last one, sequentially. The standard order of measurements is shown in Figures 2-4 and 2-5.

![Figure 2-4. Measurement of the 40 transimpedances in the hemiarray drive pattern. Each transimpedance is the ratio of the measured voltage to the injected current.](image)

<table>
<thead>
<tr>
<th>Current Electrode Pair</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1   -  -  11  16  21  26  31  -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2   -  -  17  22  27  32  36  -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3    1  -  -  23  28  33  37</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4    2  6  -  -  29  34  38</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5    3  7  12  -  -  35  39</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6    4  8  13  18  -  -  40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7    5  9  14  19  24  -  -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8    -  10  15  20  25  30  -</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

![Figure 2-5. Sequence of transimpedance measurements using the hemiarray electrode configuration.](image)
**EIT Reconstruction**

Reconstruction is the process of converting data into relevant information about the inside of the body. In EIT, the data are a time series of transimpedance measurement frames. In order to create the reconstructions, it is necessary to know the relationship between the internal conductivity of a region of the abdomen and the impedance measured at the surface.

**Difference Imaging**

The reconstruction used in this study is a difference imaging method that measures the dynamic change in conductivity with respect to a reference measurement, rather than the absolute conductivity at a single point in time (Murphy and Rolfe 1988). The resulting reconstructions show areas of increasing or decreasing impedance, rather the boundaries of internal anatomical structures like CT or US.

In difference imaging, it is assumed that at time $t_0$ there exists a conductivity distribution $\vec{\sigma}_0$ within the domain $\Omega$.

\[
\vec{\sigma}_0 = \begin{bmatrix}
\sigma_{1,0} \\
\sigma_{2,0} \\
\vdots \\
\sigma_{n_p,0}
\end{bmatrix}
\]  

(2-4)

At $t_0$ the EIT measurement frame is

\[
Z_{M0} = \begin{bmatrix}
Z_{4,0} \\
Z_{2,0} \\
\vdots \\
Z_{n_M,0}
\end{bmatrix}
\]  

(2-5)

Later, at time $t'$, the conductivity distribution changes to
\[ \tilde{\sigma}' = \tilde{\sigma}_0 + \Delta\tilde{\sigma} = \begin{bmatrix} \sigma_{1,0} + \Delta\sigma_1 \\ \sigma_{2,0} + \Delta\sigma_2 \\ \vdots \\ \sigma_{n,0} + \Delta\sigma_n \end{bmatrix}, \] (2-6)

which causes the EIT measurement frame to become

\[ \tilde{Z}_M' = \tilde{Z}_M + \Delta\tilde{Z}_M = \begin{bmatrix} Z_{1,0} + \Delta Z_1 \\ Z_{2,0} + \Delta Z_2 \\ \vdots \\ Z_{n,0} + \Delta Z_n \end{bmatrix}. \] (2-7)

The difference method is more robust to electrode misplacement and instrumentation inaccuracies that otherwise would cause artifacts using absolute imaging methods (McEwan et al. 2007). Errors shared by the reference measurement and subsequent measurements tend to be canceled in reconstructed images. The difference method assuages unavoidable limitations in systematic error, but is not cause to abandon careful attention to systematic error. Any dynamic errors are still deleterious.

Difference imaging relates the vector of transfer impedance changes measured outside the body, \( \Delta\tilde{Z}_M \), to the changes in the local conductivity within the volume \( \Delta\tilde{\sigma} \). These quantities are related by some analytic function, \( f \), according to:

\[ \Delta\tilde{Z}_M = f\left(\Delta\tilde{\sigma}\right) \] (2-8)

Equation (2-8) is called the forward problem because it relates these two quantities causally, i.e., the conductivity determines the impedance measurements.

Inversion of the forward problem gives the relationship used to reconstruct EIT images. The inverse problem requires an inverse function, \( f^{-1} \), such that

\[ \Delta\tilde{\sigma} = f^{-1}\left(\Delta\tilde{Z}_M\right) \] (2-9)
The forward and inverse problems are both challenging because they require solution of non-linear functions. The fundamental electrical law governing these problems is the Laplace equation.

**Laplace Equation**

The patient’s body forms a conductive domain, $\Omega$, with spatial admittivity distribution $\gamma(x, y, z)$. Admittivity is a complex quantity, whose real component is the electrical conductivity, $\sigma$, and imaginary component is the electrical permittivity, $\varepsilon$, according to

$$\gamma(x, y, z) = \sigma(x, y, z) + j\varepsilon(x, y, z). \quad (2-10)$$

When current is driven into the body, the domain is subject to the Neumann boundary condition

$$\gamma \frac{\partial \phi}{\partial n} = J, \quad (2-11)$$

where $J$ is the electric current density imposed at the boundary and $n$ is the vector normal to the domain surface.

The imposed electrical current creates a potential field, whose distribution, $\phi(x, y, z)$ is governed by the Laplace equation

$$\nabla \cdot (\gamma \nabla \phi) = 0. \quad (2-12)$$

If $\phi$ can be measured, then $\gamma$ can be determined by solution of (2-12) with the assumed boundary condition (2-11). Unfortunately, the Laplace equation can only be solved analytically if $\Omega$ is homogeneously conductive and has a simple geometry (Pidcock *et al.* 1995a; Pidcock *et al.* 1995b). The human body has neither a simple geometry nor a homogeneous domain. Solutions to the Laplace equation in realistic, complicated geometries require non-analytic strategies (Yorkey *et al.* 1987, Lionheart 2004).
Linearization of the EIT Reconstruction Problem

The relationship, \( f \), between \( Z_M \) and \( \Delta\sigma \) was approximated by the Taylor series polynomial expansion centered around \( \sigma_0 \) (Stewart 1999):

\[
\Delta Z_M = f(\Delta\sigma) = \sum_{n=0}^{\infty} A_n (\Delta\sigma)^n
\]

where \( A_n \) are the Taylor series coefficient matrices. If \( \Delta\sigma \) are assumed to be very small, then (2-13) can be simplified into the linear relationship:

\[
\Delta Z_M \approx A_1 \cdot \Delta\sigma
\]

where \( A_1 \) is the Jacobian matrix. This construction is ideal because it is simple, and for small conductivity changes it is accurate; however, it requires knowledge of the Jacobian matrix in order to solve the reconstruction. The Jacobian was found using two-port electrical network theory described below.

Lead Vector Theory

Having assumed the conductivity and transfer impedance changes were linearly related, the electrical compensation theorem was used to determine the Jacobian. The compensation theorem is part of two-port linear network theory, and states that an impedance change in one branch of a linear network \( \Delta Z \) is equivalent to the insertion of an independent voltage source equal to the impedance change multiplied by the current originally flowing through that branch (Papoulis 1956). The compensation theorem is illustrated in Figure 2-6. If the gain through the network from a second port to a third port is known, then those ports can be used to detect the impedance change at the first port.
An extension of the compensation theorem is given by Geselowitz (1971) and confirmed by Lehr (1972), who relate the change in the transfer impedance given a change in local conductivity according to

$$\Delta Z_M = -\Delta \sigma \int_{\Omega} \nabla V_\Phi (\sigma_0) \cdot \frac{\nabla V_\Psi}{I_\psi} (\sigma_0 + \Delta \sigma) d\Omega. \quad (2-15)$$

Assuming $\Delta \sigma$ is small with respect to $\sigma_0$, it can be neglected, resulting in a linearization of the previous relation:

$$\Delta Z_M \approx -\Delta \sigma \int_{\Omega} \nabla V_\Phi (\sigma_0) \cdot \frac{\nabla V_\Psi}{I_\psi} (\sigma_0) d\Omega. \quad (2-16)$$

If a constant current is imposed, such that $I = I_\Phi = I_\psi$, as is common in EIT, equation (2-16) can be written:

$$\Delta Z_m \approx S \Delta \sigma, \quad (2-17)$$

where

$$S \triangleq -\frac{1}{I} \int_{\Omega} (\nabla V_\Phi \cdot \nabla V_\Psi) d\Omega. \quad (2-18)$$
$S$ is the sensitivity of set of the ports $\Phi$ and $\Psi$ to the change in conductivity in a small piece of the domain, $d\Omega$. $\frac{\nabla V_{\phi}}{I}$ and $\frac{\nabla V_{\psi}}{I}$ are referred to as the lead vector fields, since they are the electric fields associated with a particular lead, or port.

The dot product (sometimes called the inner product or scalar product) indicates that sensitivity is maximized when the lead vector fields of the two ports are in the same direction, and is zero when the two fields are perpendicular. A large sensitivity is desirable because it indicates that a conductivity change in a certain area is detectable from the transfer impedance change across the given port combination.

**The Sensitivity Matrix and the Forward Problem**

When a sequence of $n_M$ measurements is made in order to determine the changes of $j$ local conductivities, equation (2-17) is usefully expressed in discrete matrix form:

$$\Delta Z_M \cong S \Delta \sigma.$$  \hspace{7cm} (2-19)

$S$ is called the sensitivity matrix, and its entries are given by

$$S_{i,j} \triangleq -\frac{1}{I_j} \int (\nabla V_{\phi} \cdot \nabla V_{\psi}) dV_j.$$  \hspace{7cm} (2-20)

$S_{i,j}$ is the sensitivity of the $i^{th}$ measurement to a change in the $j^{th}$ pixel’s conductivity. The sensitivity matrix is the Jacobian matrix in equation (2-14).

The sensitivity matrix was determined a priori. $S$ was efficiently determined by solving a single forward problem using the finite element method (FEM) as described by the method of Murai and Kagawa (1985). A commercial FEM package (COMSOL, Burlington, MA) was used to solve the forward problem. A two-dimensional and three-dimensional forward problem were both used, and subsequently compared. The two-dimensional (2D) model used a unit disc divided into 1928 quadratic, triangular pixels. The 2D model is shown in Figure 2-7.
In both cases, because the internal conductivity distribution cannot be known \textit{a priori}, $S$ was calculated assuming a uniform conductivity distribution. Meeson \textit{et al.} have shown that this is a reasonable assumption (1995). They also found that making more complicated assumptions, e.g. assuming a conductivity distribution based on typical anatomy, resulted in errors that were equal to, or greater than, those obtained from a uniform conductivity assumption.

The FEM models were solved to find the lead vector fields for relevant ports. The lead vector fields are shown in Figure 2-8. The current streamlines are shown where the line spacing is proportional to the current density. The voltage distribution is represented by the color gradient. The lead vector fields were exported to MathWorks’ MATLAB where they were used to calculate $S$ according to (2-20). Figure 2-9 shows the average sensitivity in each pixel.
Figure 2-8. Two dimensional forward problem solutions showing the lead field vector for each port in the hemiarray. The colored gradient represents the voltage distribution. The density of the current streamlines is proportional to the current density.

**Inverse Problem**

Equation (2-19) describes cause and effect, but in EIT, we wish to determine $\Delta \sigma$ given $\Delta Z_M$. This is an *inverse problem*, and it is considerably more difficult to solve than the forward problem. The inverse problem consists of estimating the constituitive parameters, $\Delta \sigma$, of the forward problem:

$$\Delta \tilde{\sigma} = S^{-1} \Delta Z_M.$$  \hspace{1cm} (2-21)

$S$ is ill-conditioned and therefore its inverse cannot be calculated easily. Further, $S$ is generally not a square matrix, i.e. the number of independently measureable impedances is not equal to the number of pixels in the reconstruction.

Because it is rectangular, $S$ is noninvertible, i.e. $S^{-1}$ does not exist. However, pseudoinversion techniques can be used to obtain an estimate of the inverse, $S^+$. Pseudoinversion
techniques are a topic of considerable length and breadth, and have been discussed more fully elsewhere (Cheney et al. 1990; Avis and Barber 1992). Regardless of the pseudoinversion used, the inverse problem becomes

$$\Delta \sigma = S^* \Delta Z_M + \epsilon$$

(2-22)

where $\epsilon$ is the residual error in the inverse solution due to ill-conditioning of $S$.

A comparison of strategies for pseudoinversion and regularization strategies for detecting IAH using the hemiarray configuration concluded that truncated singular value decomposition (TSVD) was best (Oh 2009). TSVD is a variation of singular value decomposition (SVD) that
regularizes the solution by eliminating small singular values (Hansen and O’Leary 1993). TSVD is a two step algorithm. First, S was decomposed according to SVD

\[ S = UV^* \]  

(2-23)

where \( U \) is a square unitary matrix having dimensions \( i \times i \), \( \Sigma \) is the \( i \times i \) diagonal matrix whose entries are the singular values, or eigenvalues of \( S \), and \( V^* \) is the conjugate transpose of a square unitary matrix with dimensions \( i \times j \). The columns of \( V \) are the eigenimages, or singular images, of \( S \). The eigenimages form the basis of the reconstruction images (Zadehkooshak et al. 1991).

The pseudoinverse was found according to

\[ S^+ = V \Sigma^{-1} U^* \]  

(2-24)

The root of the inverse problem is not the number of available measurements, but rather the fact that large conductivity changes deep within the domain have only a minor effect on measurements at the surface. This is quantifiable using the condition number,

\[ \kappa(S) = \frac{\Sigma_{\text{max}}(S)}{\Sigma_{\text{min}}(S)} \]  

(2-25)

where \( \Sigma_{\text{max}}(S) \) and \( \Sigma_{\text{min}}(S) \) are the maximum and minimum singular values of \( S \), respectively. Ideally, the condition number should be one. Large condition numbers indicate that a matrix is ill-conditioned, meaning it is nearly singular. The condition numbers for the 2D and 3D reconstruction matrices were \( 6.4548 \times 10^{17} \) and \( 1.2835 \times 10^{17} \), respectively.

Equation (2-24) gives the full-rank \( S^+ \), using SVD. Next, regularization was applied by replacing the smallest singular values with zeroes. The number of remaining singular values is called the regularization parameter, \( k \).

The regularization parameter was chosen using the \( l \)-curve method (Hansen and O’Leary 1993). The \( l \)-curve plots the norm of the solution against the norm of the residual error for all valid regularization parameters.
The $l$-curve depends on the measurement, and selection of regularization parameters, depends on the measurement and its level of noise. Using the average of the columns of $S$ as a synthetic, noiseless measurement the $l$-curve regularizations parameters ranging from $k = 8$ to $k = 16$ would be useful, as shown in Figure 2-10. Unless otherwise noted, $k = 12$ was used in this study.

The condition number can be reduced by normalizing the sensitivity matrix using a weighting scheme. The weighted minimum norm (WMN) method proposed by Clay and Ferree preconditions the sensitivity matrix before it is inverted. Using WMN, the inverse problem becomes

$$\Delta\sigma = W(SW)^+ \Delta Z + \epsilon$$

where the weighting matrix, $W$, is the diagonal matrix

$$W = \text{diag}(\overline{w}_j)$$

whose entries are

$$w_j = \left( \sum_{i=1}^{m} S_{i,j}^2 \right)^{-1/2}$$

This weighting method normalizes the spatial sensitivity, improving the sensitivity of voxels deep to the location of the electrodes. Using WMN, the condition number of the sensitivity matrix was reduced to $1.9127 \times 10^{17}$. 

47
Quantification Using EIT

The difficulty in solving the inverse problem means the EIT images suffer from poor resolution, incorrect localization, and artifacts due to noise. Despite their poor quality, it was possible to extract useful parametric data from the images. By integrating the local conductivity changes, an estimate of the overall conductivity change, called the Quantity Index (QI) is obtained:

$$\text{QI} = \sum_{j=1}^{n_p} A_j \cdot \Delta \sigma_j.$$  \hspace{2cm} (2-29)

Here $A_j$ is the area of the $j$th pixel, and $n_p$ is the total number of pixels in the reconstruction. In 2D, QI has units of Sm (or m/Ω). 

Figure 2-10. Synthetic $l$-curve.
QI is the total conductivity change within an EIT reconstruction. QI extracts a parameter from the reconstructed image, and the image itself is relegated to a secondary role in confirming the plausibility of the QI estimate. QI is useful because it parameterizes and quantifies the reconstruction image, giving a value that can used both to determine the most optimal algorithm, and can be used to automate the detection of IAH. QI is also useful when the reconstruction noise is evenly distributed around zero, such that the summation process cancels out noise contribution.

The QI value depends, in part, on the reconstruction method. Different combinations of regularization, preconditioning and pseudoinversion will have an effect on the QI. The reconstruction algorithm that results in the highest quality images may not necessarily give the optimal QI. In this study, the reconstruction method that minimized the standard deviation of the QI was deemed to be best.

The derivative of QI was expected to be proportional to the mass flow rate. Differentiating QI to obtain \( \frac{dQI}{dt} \) was not trivial due to the presence of noise. Ideally, \( \frac{dQI}{dt} \) would be found by

\[
\frac{dQI}{dt}(t) = QI(t) - QI(t-1)
\]

but this method was dominated by high frequency noise in QI.

Another option was to increase the time span of the derivation

\[
\frac{dQI}{dt}(t) = \frac{QI(t) - QI(t-d)}{d}
\]

where \( d \) is some delay. This method is less sensitive to high frequency noise, but it neglects potentially useful data during the delay, \( d \). Without that intermittent data, the delay was unnecessarily long to obtain a useful result.
A third option was to use least-squares linear regression to estimate the slope from a set of QIs. This method was insensitive to high frequency noise, and included all the available QI information.

\[
d\frac{QI}{dt}(t) = \frac{d \sum t \cdot QI - \sum t \sum QI}{d \sum t^2 - (\sum t)^2}
\]  

(2-32)

A summary of the proposed IAH detection algorithm is as follows. First, a frame of transimpedance measurements was collected. This frame was multiplied by the reconstruction matrix, known \textit{a priori}, to determine the vector of local conductivity changes. Those conductivity changes were then integrated to get a QI value. The process is repeated until a collection of \textit{d} frames, and their QIs, were assembled. The trend in the QIs was extracted using linear regression, yielding the \(dQI/dt\). This value was compared to a threshold value to determine whether or not IAH was present.
CHAPTER 3
EPACK2 DESIGN AND COMPARISON

The EPack was a prototype EIT data acquisition system designed for use with the hemiarray electrode configuration. EIT systems made by other groups were not adaptable to this configuration because those systems used more than eight electrodes and did not have architecture flexible enough to use the hemiarray adjacent drive pattern.

Architecture and Strategy

The main tasks for EIT hardware are distribution of current to the transmit (drive) electrodes and measurement of the voltages at the receive (recording) electrodes. EIT systems can be classified based on the amount of hardware used to accomplish these tasks.

Serial EIT systems have one current source and one voltmeter (Barber and Brown 1984). Switching is used to assign the terminals of the current source and voltmeter to the appropriate electrodes. This design is advantageous because it minimizes the amount of analog hardware and allows flexibility in the use of the electrodes (Yerworth et al. 2002), but it also has disadvantages. Multiplexing increases the length of time required to make measurements, and introduces parasitic capacitances in the signal chain (Brown and Seagar 1987). Serial systems are best suited for small, portable EIT applications that are robust to inaccuracies (Cusick et al. 1994).

On the other extreme, parallel EIT systems have a current source and voltmeter at each electrode (Wilson et al. 2001). These systems are able to acquire data more rapidly than serial systems because the voltage measurements can be recorded simultaneously. They also avoid the parasitic components introduced by switching; however, these systems require additional instrumentation that gives them a real appetite for power. The high data throughput generated by a parallel system necessitates a distributed digital architecture. In some systems, a separate
processor is dedicated to each electrode, with a common digital backplane receiving the preprocessed data (Oh, Woo and Holder 2007). Each current source and voltmeter must be carefully calibrated to the others to ensure system accuracy. The calibration circuitry can be cumbersome and the process is tedious (Oh *et al.* 2007). Another problem with parallel systems is lack of flexibility. Without switches, the drive pattern is fixed.

Intermediate-parallel systems are a hybrid that have parallel voltage measurement and serial current drive for a compromise of speed, power efficiency and accuracy (Rosell *et al.* 1988; Riu *et al.* 1996).

**Hardware Requirements**

**Noise Analysis**

Noise, any interfering signal contributing to measurement imprecision, limits the precision of any measurement, but the ill-posed reconstruction problem in EIT exacerbates noise. The effect of noise appears as artifacts in the reconstructed image, and resulting imprecision in QI.

Electrical noise in EIT systems originates from six noise source classifications (Fabrizi *et al.* 2007):

Thermal noise is white noise exhibited by all resistive elements. The Johnson-Nyquist equation gives the equivalent RMS voltage source:

\[
V_{th} = \sqrt{4kTB}R
\]  
(3-1)

where \( k \) is Boltmann’s constant (1.38e-23 J/K), \( T \) is the temperature in Kelvin, \( B \) is the bandwidth and \( R \) is the resistance. The transfer impedance itself has an inherent thermal noise that is unavoidable, but small. Thermal noise is also present in the current source and voltmeter components.
Quantization noise is caused by the limited precision of mixed signal (analog-to-digital, digital-to-analog) techniques. The quantization noise spectral density is

$$v_{\text{NQ}} = \frac{A}{2^b \sqrt{12f_s}}$$

(3-2)

where $A$ is the full-scale voltage, $b$ is the number of digital bits, and $f_s$ is the sampling frequency (Saulnier 2005).

Electromagnetic interference (EMI) emanates from nearby electromagnetic devices. In a modern medical environment, one can expect interference from a multitude of electronic devices. Additionally, digital components in the EIT system itself can create noise that infiltrates the analog subsystem. Power lines are another source of EMI, whose interference is usually within a well-specified bandwidth of 50-60 Hz. Electrophysiological processes can also give rise to interfering signals.

**Current Source Requirements**

The constant current source (CCS) was the first subsystem in the analog signal chain. Its function was to deliver excitation energy to interrogate the impedance of the abdomen. While it is theoretically possible to use constant voltage sources instead of a CCS, the safety of applying electrical current *in vivo* is limited by the magnitude of applied current, not the voltage (Olson 2010). At frequencies near DC, small amounts of current are potentially harmful. As frequency rises to several kilohertz the body can safely tolerate more current. The amount of current that is safely applied through the body is proportional to the operating frequency, $f_o$ (Lionheart, Kaipio and McLeod 2001). IEC60601-1 specifies a maximum current of 100uA at low frequency, 100$f_o$ nA at from 1 kHz to 100 kHz, and 10 mA maximum at higher frequency (2005). The EPack CCS was designed within these limits.
The amount of current delivered by the current source must be independent of its load. In addition to the impedance to be measured, the current source drove two electrode contact impedances that drift with temperature, pressure, and age (Boone and Holder 1996). Because the electrode contact impedance is unknown and variable, the precision of the impedance measurement is limited by the output impedance of the current source. The current source output must be constant despite variations in the electrode contact impedance; otherwise, the bioimpedance cannot be precisely measured. Imperfections in the current source are directly translated to the transimpedance estimate.

It would be possible to compensate for limitations in the current source by measuring the injected current directly, but the current sensing apparatus would need a higher precision than the current source itself. Otherwise, additional uncertainty would be added to the measurement. Therefore, it was desirable to use a current source with near-ideal behavior because it eliminated the need to measure the injected current.

**Voltmeter Requirements**

The common-mode rejection ratio (CMRR) of the voltmeter is important because large common mode voltages are typical in EIT. There are several sources that contribute to the common-mode voltage. Power-lines are a significant source of 60 Hz common mode interference. Imbalances in the electrode contact impedance, multiplexor on-impedance, and other signal path components also contribute to common mode voltages (Boone and Holder 1996). Imbalances in the current source can also give rise to common mode current injection. In floating systems, like the EPack, the common-mode voltage can be as large as 2V (Riu et al. 1990).

CMRR of EIT voltmeters can be improved using several strategies. Obviously, efforts should be made to introduce symmetry into signal chain components. High input impedance to
the amplifier helps to minimize the effects of signal chain imbalances, but input impedance is typically diminished with frequency due to parasitic input capacitance. Common-mode feedback (CMFB) can be used to reduce the common-mode signal, but this requires an additional, dedicated electrode (Rossell and Riu 1992).

**EPack**

The first generation EPack, EPack1, was developed in 1998 as a prototype, bench-top device used to evaluate the feasibility of the hemiarray configuration in simple phantoms (Tang et al. 2006). The EPack1 architecture is shown in Figure 3-1. The first generation device had a number of problems including slow acquisition speed, noisy data, and a lack of safety features required for *in vivo* operation. The second generation device, EPack2, was developed to address

**EIT101A Rev-A**  
*Block Diagram*

![EIT101A Rev-A Block Diagram](image)

Figure 3-1. EPack1 System Diagram.
shortcomings in EPack1’s performance.

The design strategy for the EPack emphasized rugged portability by using a small number of high-quality components. A low component count has direct benefits in terms of space savings and cost, and secondary benefits in terms of fewer supporting components, less power consumption, heat generation and calibration. Wherever possible, the EPack employs simple, effective instrumentation constructed with small package integrated circuits (ICs).

The EPack’s portable design strategy should be contrasted with other recently developed EIT instruments that maximize accuracy and precision without limitations on the physical size or complexity of the device. These systems are suited to different applications, such as cancer screening, in which portability is not an important factor. For example, the KHU Mark1 system, developed by the Impedance Imaging Research Center (IIRC) at Kyung Hee University, South Korea is an intermediate parallel system that achieves SNR of over 100 dB. The elaborate instrumentation consumes enough power to require a separate, specially designed power supply capable of delivering as much as 10A. Furthermore, the system must be calibrated before each use to obtain the published results (Oh et al. 2007b).

Another elaborate EIT system is the ACT-4, which uses the adaptive current pattern and has a parallel architecture. The ACT-4 achieves SNR over 100dB and can make about three measurements each second (Saulnier et al. 2007); however, this system is large enough to require a wheeled cabinet.

Parallel systems are more precise than their serial counterparts are. However, the ongoing proliferation of improved analog IC technology justifies the re-examination of the serial architecture’s capabilities. For example, the CardioInspect system developed at Tel Aviv University has a compact serial architecture that achieves 75dB SNR (Zlochiver et al. 2007).
Furthermore, the development of appropriately robust reconstruction and post-processing techniques may relax the stringent performance requirements.

The goal in developing the second generation device was to focus on safety issues while minimizing unnecessary changes to the EPack1 in order to shorten development time. The following six major changes to EPack1 were proposed and implemented. First, preamplifiers were added to the front end of the voltmeter. Second, safety was improved by adding DC-blocking networks at interfaces between the patient and the device. Third, the multiplexing circuitry was replaced with a more modern system that was flexible and required less circuitry. Next, the differential amplifier was replaced with one that had better performance. The digital communications were entirely revamped to increase reliability. The final improvement was the reduction of the supply voltages from ±15 V to ±5 V, in an effort to conserve power. These improvements resulted in an improved, streamlined EPack2 system, illustrated in Figure 3-2. In the following section, the design of these improvements, and the overall function of EPack2, are detailed.

**Analog Hardware**

The EPack’s analog signal chain included the current source and the voltmeter, a multiplexor used to address these peripherals among eight electrode channels, and front-end circuitry to interface safely with the patient.

**Constant Current Source**

The current source in both EPack generations consisted of a waveform generator, a voltage-to-current converter, and a switching system that distributed current among the eight electrodes.
Waveform generation

Most current source topologies are a type of voltage controlled current sources that convert a voltage waveform input into a proportional output current. The synthesis of the voltage waveform is critical since it is at the beginning of the signal chain.

The EPack used direct digital synthesis (DDS) to drive the current source. DDS is a stable method of synthesizing analog waveforms using a ROM lookup table and a digital-to-analog
converter (DAC). DDS allows tremendous flexibility in selection of the operating frequency and waveform shape, but here only pure tone sinusoids are used.

The Analog Devices AD9850, a monolithic, programmable DDS integrated circuit (IC) was used. This DDS had a fully differential, sinusoidal output whose frequency and phase are programmable via a serial digital interface. The frequency was set using a 32-bit value that scales the reference clock, which was supplied externally. The reference clock used in the EPack2 was 33 MHz, therefore the frequency could be set as high as 33 MHz in 0.0076 Hz increments.

EPack2 was designed to run at four user-selectable frequencies: 15.625 kHz, 31.25 kHz, 62.5 kHz and 125 kHz. These selections were convenient to the digital architecture but are otherwise arbitrary. 62.5 kHz yielded good results for bleeding detection with that unit.

**Howland voltage controlled current source**

Many types of current source topologies have been used in bioelectrical studies, but the Howland source remains a popular choice since it can be constructed using a single operational amplifier (opamp) and a handful of resistors (Sheingold 1964). Studies have shown that the Howland has comparable performance to other, more complicated, current sources (Filho, Brown and Wilson 2000). Other authors have suggested that the Howland cannot have high output impedance at EIT frequencies (Hong et al. 2009); however, this is not the case when the circuit is designed carefully.

Several variations of the Howland have been used in neural stimulation (Pouliquen Vogelstein and Etienne-Cummings 2008), tissue characterization (Bertemes-Filho 2002), single-electrode capacitive sensors (Chen, Deng and Yang 2010), and EIT (Ross et al. 2003; Oh, Woo and Holder 2007).

Current mirror or current conveyor topologies have also been used successfully in EIT. For example, Bragós et al. created a type two current conveyor (CCII) using the AD844 current...
feedback amplifier (1994). These topologies are a more natural approach because they operate using current-mode elements that have high impedance output ports (Denyer et al. 1994; Jivet and Dragoi 2008). A comparison of CCII and Howland topologies concluded that the CCII has a slightly better performance than the Howland topology, but neither topology could exceed 1 MΩ at high frequencies (Bertemes-Filho et al. 2000).

Both EPacks were designed to allow a swappable current source. The current source was the only component from EPack1 that was entirely unmodified in EPack2, due to the careful attention required to properly redesign it. The current source used in EPack1 and EPack2 was a bipolar Howland current source (BHCS) with a negative impedance converter (NIC) (Bertemes-Filho et al. 2004). This circuit consisted of two independent Howland generators, and two NIC circuits that boosted the output impedance by canceling capacitance in the multiplexer. The complete circuit schematic is shown by Figure 3-3. This design was intended for serial EIT architectures.

Figure 3-3. Schematic of Bipolar Howland Current Source with Negative Impedance Converters
The performance of the CCS suffered from inattention to the fundamental requirements of this topology, most notably resistor mismatch greater than 5%, and poor selection of opamps (LM833). As shown in Figure 3-4, the circuit was constructed on a single sided printed circuit board (PCB) using large DIP components and sockets, long wires, and no power planes for noise shielding. The output impedance of the current source was calculated by measuring the voltage developed across a load resistor connected to the terminals of the CCS. The load was varied from 270 Ω to 3.3 kΩ. The voltage was measured using an oscilloscope with 1MΩ input impedance. This strategy would not obtain accurate results for a better CCS; however, the oscilloscope input impedance is sufficiently large in this case. The output resistance was measured to be about -67 kΩ, far below specification. However, given the time constraints of this project, other improvements were more critical.

Figure 3-4. Photograph of Bipolar Howland Current Source with Negative Impedance Converters. Photograph courtesy of Aaron Tucker.
Front End

The EPack frontend consists of those components that are directly interacting with the patient. The frontend components of EPack2 were the multiplexers, DC-blocking networks, shield drivers, and preamplifiers. The frontend was redesigned to improve the system’s safety as described below.

Crosspoint multiplexer

The EPack required a multiplexer that can distribute four peripheral channels (two for the current source, and two for the voltmeter) among eight electrode channels (a 4-to-8 multiplexer).

EPack1 used Analog Devices ADG408 8-to-1 analog multiplexors. A functional schematic of the switch is shown in Figure 3-5. The ADG408 was replaced for several reasons. First, it was occupying too much PCB space. The IC was only available in a relatively large dual inline

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Figure 3-5. Functional schematic of Analog Devices ADG408 8-1 analog multiplexer.
package (DIP) that used a lot of PCB space. This was compounded by the fact that an array of four ADG408 were required to build a multiplexer with the required number of channels, and further worsened by the external, dedicated “glue” logic that was used to decode digital selection of the multiplexers. In total, seven DIP ICs were dedicated to the multiplexer. Additionally, the ADG408 had 56pF of on-capacitance, which was very large compared to other alternatives. This large capacitance was one of the reasons the EPack1 multiplexers required as long as 250 ns to switch. Finally, because the multiplexers had to be controlled separately, it was not possible to quickly disconnect the patient from the current source. This meant there was a brief period of time when one side of the current source was connected to the patient and the other side was disconnected. Under this condition current would be forced to flow through the patient to ground, which was unpredictable and undesirable for safety.

EPack2 replaced the multiplexers with the Intersil CD22M3494 8-to-16, bidirectional crosspoint switch. Figure 3-6 shows the functional schematic of the crosspoint switch. For flexibility, two crosspoints were used. One was dedicated to the current source and the other was dedicated to the voltmeter. Unused channels were reserved for testing and debugging purposes. The crosspoint switches were more flexible than multiplexers, allowing any arbitrary combination of channels to be connected.

The crosspoints were controlled using a parallel digital interface. Seven bits were used to select a combination of input and output channels, and an eighth bit was used to either make a connection or break it. The crosspoints also had a reset line that simultaneously broke all connections, and a chip-select input that made it easy to share digital control between the two crosspoints.
Figure 3-6. Functional schematic of Intersil CD22M3494 16-8 analog crosspoint switch.

The CD22M3494 had a maximum on-capacitance of 20pF, which was much smaller than the previous multiplexer’s. The crosspoint was available in a compact plastic leadless chip carrier (PLCC) package that conserved PCB space. Most importantly, the crosspoint chips required only 60 ns to turn on, a quarter of the time required by the previous multiplexer. The ability to simultaneously break all connections also gave a speed and safety improvement.

**DC-blocking network**

The EPack1 current source had a DC offset on the order of 10 μA, which was near the safety limit for *in vivo* operation. This DC current was blocked using a high-pass RC filter. Polystyrene capacitors were chosen for their large breakdown voltage, low dielectric absorption, and overall reliability. The resistor was set to be large so as not to further degrade the current source output impedance.

**Shield driver**

The EPack was connected to the electrodes using coaxial cables. Usually, in a coaxial cable the shield conductor would be grounded to absorb EMI, but in EIT coaxial capacitance between the conductor and shield provides a stray current path that diverts current that should be
flowing through the patient. The coaxial cable’s distributed capacitance reduces the precision of
the excitation current. This capacitance is on the order of 20 pF, but is also problematic because
it changes as the cable is bent or twisted.

Instead of fixing the coaxial shield to ground, an opamp voltage follower was used to drive
the shield at the same voltage as the coaxial conductor. Because the same voltage was applied at
both sides of the cable capacitance, no current flowed through it, i.e. the cable capacitance was
bootstrapped. This method was still effective for shielding against EMI because the buffer
amplifier had low output impedance.

The design of the shield driver is not trivial, although the op-amp voltage follower
configuration is a familiar one. The op-amp needs to have sufficiently high open-loop gain and
gain-bandwidth to effectively bootstrap at EIT frequencies. This requirement is not particularly
stringent because the op-amp is in a low gain configuration; however, this also means that
stability is an important concern, especially because the op-amp is driving a capacitive load.
Instability in the shield driver will introduce significant noise in the EIT measurement, and
external compensation may be necessary for some op-amps. Finally, as was previously
mentioned, the op-amp should have low output impedance for effective EMI shielding. EPack2
used the National Semiconductor LF353, which met the aforementioned requirements.

For patient safety, a high-pass network at the output of the patient shield to prevented DC
current flow should the patient contact the shield. The same DC-block network used for the
current source was used for the shield driver. An alternative solution would be to insulate the
shield from the patient.

**Voltmeter preamplifier**

Long cables or PCB traces connecting the electrodes to the rest of the analog
instrumentation will introduce losses, reduce the CMRR and receive EMI. These distances
should be minimized, but the electrode spacing guarantees that long runs are unavoidable. Preamplification was therefore necessary.

Preamplifiers (preamps) preserved signal quality and maintained patient safety. The preamps presented a high input impedance at the voltmeter front-end to minimize current flow from the body into the instrumentation. The preamps blocked the flow of DC, which can cause irritation or burning even in small amounts. The high input impedance of the preamps also minimized measurement error in the voltmeter caused by loading and high common-mode voltages. The preamp output was a low impedance path to ground for EMI. Finally, the preamp drives the multiplexer switches and instrumentation amplifier in subsequent stages of the signal path. Therefore, the preamp required ac-coupling at the input, high input impedance, and low noise figure.

The bootstrapped AC follower was used as the preamplifier (Murphy and Rolfe 1988). The schematic of the preamplifier is shown in Figure 3-7. For an ideal op-amp, the input impedance of the circuit is infinite. In practice, the input offset voltage of the op-amp, finite open-loop gain and gain-bandwidth, and parasitic capacitances associated with the op-amp and the PCB layout limit the input impedance at EIT frequencies.

The input referred noise of the preamp was dominated by selection of the op-amp. Studies have shown that the thermal noise contributed by the relatively large bias resistors was smaller than what would be expected based on simple models of thermal noise (Vargas and Pallas-Areny 1994).

**Voltmeter**

The voltmeter measured the potential difference between two points on the surface of the body. The first stage of the voltmeter was an amplifier that received differential inputs signals selected by the multiplexer, subtracted them, and converted them to a single-ended signal. The
The second stage was an analog-to-digital convert (ADC) that digitally estimated the amplified voltage and reported the measurement to the digital processor.

**Instrumentation amplifier**

The function of the instrumentation amplifier (in-amp) was to receive a differential signal pair selected by the multiplexer, subtract the signals, and apply gain. The subtraction canceled out common mode signal, likely to be noise, and the gain prevented the output signal from being corrupted by noise in subsequent signal chain elements.

EPack1 used the Burr-Brown PGA202KP in-amp. This in-amp had digitally controlled, variable gain and had good performance; however, it required ±15 V power supplies. EPack2 had smaller power rails, and therefore the Analog Devices AD621 was selected as a replacement. This in-amp only required a single 5V power supply, had low drift and otherwise similar performance compared with the PGA202KP. To accommodate the input voltage range, the in-amp was powered by bi-polar ±5 V supplies. One drawback was the AD621 had less flexibility in its programmable gain. To simplify design, the gain was fixed to 20 dB.
The in-amp outputted a single ended signal that was measured by the ADC. The DC offset of the in-amp output was controlled by a 2.5 V reference supplied from the ADC. The offset was necessary because the ADC expects a signal that varies from 0 V to 5 V. The conversion was insensitive to variations in the voltage reference because it was used as the reference for the conversion as well.

**Analog-to-digital converter**

The ADC was the last stage in the analog signal chain. EPack2 retained the same ADC used in the first generation EPack, the Analog Devices AD9240. This ADC operated on a single 5V power supply and consumed as much as 300 mW.

The ADC sampled at up to 10 MHz and converted voltages to 14-bit digital values. The actual sample speed was controlled by the digital system to maintain 32-times oversampling regardless of the current source operating frequency. Typically, the current source operated at 62.5 kHz and the ADC sampled at 2 MHz.

**Digital Hardware**

**Digital Signal Processor**

Operation of the EPack was controlled and synchronized by a digital signal processor (DSP). Both EPack generations had an ADSP-2181 (Analog Devices), a 16-bit fixed-point processor. The DSP controlled the operation of the DDS, switches, and ADC. Data received from the ADC was processed, and transmitted to a personal computer (PC) via communication link.

**ADC Interface**

The ADC clock was generated using one of the ADSP-2181 internal SPORT peripherals. The SPORT peripherals included clock signal generators intended for use with synchronous serial communications. These clocks were used to drive the ADC clock.
ADC data were received using the direct memory access (DMA) interface. DMA operation was initialized by the state machine, which set a pointer at the beginning of the memory allocated for ADC data. The ADC clock doubled as a trigger for the DMA interrupt, signaling the DMA interface that a new ADC result was available. After being triggered by the clock, the DMA controller wrote the ADC result to memory, and incremented the DMA pointer to the next memory address. Meanwhile, the state machine monitored the address of the DMA pointer to determine when the total number of ADC samples had been received.

**Embedded Data Processing**

For each measurement a total of $n_S$ samples were recorded. These samples record the sinusoidal response over a period of $n_C$ cycles at the injection frequency $f_O$.

$$v_{in} = \hat{v}\cos(2\pi f_O + \theta) + v_{DC} \tag{3-3}$$

The average amplitude of the voltage waveform was estimated digitally as the AC root-mean-square (RMS) value of the waveform, which was related to the amplitude of the waveform, $\hat{v}$, according to:

$$v_{RMS} = \sqrt{\frac{1}{n_S} \sum_{i=0}^{n_S} (v_i - \overline{v})^2} = \frac{\hat{v}}{\sqrt{2}} \tag{3-4}$$

where $v_i$ was the $i^{th}$ digital sample, and $\overline{v}$ was the average sample value, or DC offset.

The EPack only sent the amplitude information for each measurement, rather than the entire sampled waveform. This significantly reduced the required data throughput from the EPack to the PC. A single value for each measurement was transmitted rather than the entire sampled waveform. If an error was suspected, the original waveform could be transmitted over the communication link for inspection.
The first step was an ensemble averaging over the $n_C$ recorded cycles. For uncorrelated, white Gaussian noise, this reduced noise by a factor of $\sqrt{n_C}$, yielding an SNR improvement of $10\log(n_C)$ dB. However, averaging did not boost SNR as much as expected, most likely because the predominant noise was systematically correlated. After ensemble averaging, a single period of the waveform was used for RMS estimation. To improve efficiency, only the first step of the RMS calculation was performed on the DSP. The sum-square, $x_{SS}$, was calculated as

$$x_{SS} = \sum_{i=0}^{n_c} (x_i - \bar{x})^2,$$

where $x_i$ was the $i^{th}$ digital sample, and $\bar{x}$ was the average sample value, or DC offset.

Computationally intensive operations required to complete the estimation of $\hat{v}$ were performed on the laptop.

**Digital Communications**

**Hardware layer**

The ADSP-2181 had a general purpose serial interface that required a considerable amount of software control to generate RS-232 compatible signaling. Therefore, both EPack1 and EPack2 instead used an external 16C550 universal asynchronous receiver/transmitter (UART), interfaced via the DSP’s external memory interface bus.

EPack1 had a RS232 standard D-sub connector which connected to a PC using a standard 9-wire serial cable. For wireless communication, EPack1 had an RF radio that did not have reliable performance.

Since many modern PCs no longer have RS-232 compatible serial ports, the EPack2 was redesigned to be compatible with modern serial communication protocols. For wired connections, EPack2 included the FTDIChip FT232R UART-to-USB Bridge that allows
communication over a standard USB 2.0 port. FTDIChip includes a virtual COM port (VCP) driver for the PC that interfaces the USB connection to legacy software built on the RS232 platform. On the EPack2 there were transmit and receive LEDs indicating the status of the USB communications.

The wired connection between the EPack and the PC was isolated to prevent potentially dangerous currents from being exchanged between the two systems. The Texas Instruments ISO7221B digital isolator was used to provide an isolation barrier between the DSP and the FT232R. Half of the digital isolator was powered from the EPack2 power supply. This side interfaced with the UART on the EPack2. The other half of the isolator and the FT232R circuitry were powered by the USB host machine. A large isolation gap was also designed into the PCB to maintain the separation of the two power systems.

EPack2 had a female, USB Type-A standard connector for simplicity. Using the USB interface, EPack2 can transmit data at baud rates up to 115 kbps.

For wireless applications, the EPack2 had a BlueSMiRF UART-to-Bluetooth bridge that also operates at baud rates up to 115 kbps. The Bluetooth link was not authorized for in-hospital use due to concerns of interference with 802.11b/g wireless internet networks used by clinicians; however, in-lab testing showed no problems with interference between the wireless standards. An advantage of Bluetooth was that it did not require a physical connection to the host machine and therefore it included the necessary isolation; however, the Bluetooth modem consumed more power than USB communications. USB or Bluetooth operation was selectable by a jumper on the PCB.

**Software layer**

A bi-directional (full duplex) data protocol was designed to allow a remote master device to control the EPack. The EPack acted as a slave that received predefined function commands,
executed the command, and returned relevant data to the master device. Figure 3-8 lists the commands that the EPack recognized. Commands and data were encapsulated into a data packet designed to increase reliability. The data packet includes framing, the datalength, a checksum, and other information relevant to the embedded state machine. When invalid command or data packets were received, devices exchanged NACK packets, indicating the need for retransmission. Successfully received information was acknowledged via an ACK packet. This helped identify and automatically correct communication errors but contributed overhead that reduced data throughput.

<table>
<thead>
<tr>
<th>Command Name</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PINGID</td>
<td>1</td>
<td>Ping</td>
</tr>
<tr>
<td>VPAIRD</td>
<td>2</td>
<td>Manual Voltage Pair Selection</td>
</tr>
<tr>
<td>CPAIRD</td>
<td>3</td>
<td>Manual Current Pair Selection</td>
</tr>
<tr>
<td>FREQID</td>
<td>6</td>
<td>Manual Set Operating Frequency</td>
</tr>
<tr>
<td>SINGLEID</td>
<td>10</td>
<td>Single Transimpedance Measurement</td>
</tr>
<tr>
<td>COMPLID</td>
<td>11</td>
<td>Complete Transimpedance Measurements</td>
</tr>
<tr>
<td>KILLID</td>
<td>12</td>
<td>Abort Current Measurement</td>
</tr>
<tr>
<td>TIMEID</td>
<td>31</td>
<td>Get Internal Timer Value</td>
</tr>
<tr>
<td>VERSID</td>
<td>32</td>
<td>Get Firmware Version</td>
</tr>
<tr>
<td>RESETID</td>
<td>50</td>
<td>Reset to Default Configuration</td>
</tr>
<tr>
<td>ENDEBUGID</td>
<td>51</td>
<td>Enable</td>
</tr>
<tr>
<td>ITESID</td>
<td>53</td>
<td>Manually Turn on Current Source (Debugging)</td>
</tr>
<tr>
<td>WAVEDATAID</td>
<td>54</td>
<td>Report data as unprocessed sampled waveforms</td>
</tr>
<tr>
<td>RMSDATAID</td>
<td>55</td>
<td>Return RMS value of measurements</td>
</tr>
<tr>
<td>VTESTID</td>
<td>60</td>
<td>Manually test Voltmeter (Debug)</td>
</tr>
<tr>
<td>BUSYID</td>
<td>87</td>
<td>Error: Processor is Busy</td>
</tr>
<tr>
<td>DEEUGID</td>
<td>88</td>
<td>Reserved for Debugging</td>
</tr>
<tr>
<td>INTRID</td>
<td>89</td>
<td>Error: Internal error</td>
</tr>
<tr>
<td>INVCOMID</td>
<td>90</td>
<td>Error: Invalid command</td>
</tr>
<tr>
<td>CSERRID</td>
<td>91</td>
<td>Error: Invalid Checksum</td>
</tr>
<tr>
<td>INVLENID</td>
<td>92</td>
<td>Error: Invalid Packet Length</td>
</tr>
<tr>
<td>TIMEOUTID</td>
<td>93</td>
<td>Error: Timeout</td>
</tr>
<tr>
<td>NOHEADID</td>
<td>94</td>
<td>Error: Missing Header</td>
</tr>
<tr>
<td>INVDATAID</td>
<td>96</td>
<td>Error: Invalid Data</td>
</tr>
<tr>
<td>NACKID</td>
<td>97</td>
<td>Not Acknowledged</td>
</tr>
<tr>
<td>ACKID</td>
<td>98</td>
<td>Acknowledged</td>
</tr>
</tbody>
</table>

Figure 3-8. List of EPack2 commands.
The data packet structure in EPack2 was modified to reduce overhead. The header was reduced from five bytes to one byte, and unnecessary framing information was removed. Figure 3-9 summarizes the changes in the communication protocol.

The data protocol was tested by simulating several types of communication errors. The protocol was tested against incomplete data transmission, one and two bit data errors, and nested transmission of data packets. The protocol was able to automatically recover from all these scenarios.

**Graphical User Interface**

The EPack was controlled using a graphical user interface (GUI) written in Visual C# 2008 (Microsoft, Redmond, VA). The operator used the GUI to initiate measurements, receive data, and view live reconstructions. The software was designed to be simple, fast and intuitive. A screenshot of the GUI is shown in Figure 3-10.

**Data Processing**

The first part of the impedance calculation, calculation of $x_{ss}$, was performed on the DSP.

---

**EPack1:**

![EPack1 Packet Structure](image)

**EPack2:**

![EPack2 Packet Structure](image)

**Key:**

- **CKSUM**: Checksum
- **IDH, IDL**: High and low bytes of two-digit command ID
- **LEN**: Number of data bytes
- **DATA**: Variable length data payload
- **CR**: Carriage Return
- **LF**: Line Feed

Figure 3-9. Comparison of the EPack1 and EPack2 data packets.
in the EPack2. The laptop received $x_{ss}$ values from the EPack and calculated the measured transimpedance for each value. First, the RMS calculation and ensemble averaging were completed, giving an average, digitized RMS value

$$x_{RMS(Avg)} = \frac{1}{n_c} \sqrt{\frac{x_{ss}}{n_s}} \quad (3-6)$$

Next, the digital RMS value was converted to an analog value, accounting for the gain introduced by the instrumentation amplifier, $A_{IA}$.

Figure 3-10. Screenshot of the EPack Control Center GUI.

74
\[ V_{RMS\,(Analog)} = \frac{V_{ADC}}{2^{n_B} - 1} \frac{x_{RMS}}{A_{IA}} \]  

(3-7)

where \( n_B \) was the number of bits in the ADC. Finally, the voltage amplitude can be determined by rearranging Equation (3-4)

\[ \hat{v} = V_{RMS} \sqrt{2} \]  

(3-8)

To increase calculation efficiency, the conversion factor, \( \xi \), was predefined in PC memory:

\[ \xi = \frac{V_{ADC}}{A_{IA} (2^{n_B} - 1) n_C \sqrt{n_S}} = \frac{\sqrt{2}}{2621280} \]  

(3-9)

This allowed for a two-step conversion from \( x_{SS} \) to \( \hat{v} \):

\[ \hat{v} = \xi \sqrt{x_{SS}} \]  

(3-10)

Packaging

The EPack1 PCB and external enclosure are shown in Figure 3-12 and 3-13, respectively. The redesigned EPack2 was considerably smaller than its predecessor. Figure 3-14A shows the revised PCB, which was much smaller than the first iteration despite containing significant improvements to safety and performance. A watertight enclosure was designed to house EPack2, shown in Figure 3-14B, measuring 10 x 6 x 3 inches, compared to EPack1 which measured 9 x 9 x 4 inches. The total volume of EPack2 was 45% smaller than its predecessor and its footprint was 26% smaller.

EPack2 was inspected and approved for experimental \textit{in vivo} operation by the University of Florida Institution Review Board (IRB-01) and the Shands Hospital Department of Clinical Engineering.
Figure 3-11. EPack1 PCB. Photograph courtesy of Aaron Tucker.

Figure 3-12. EPack1 enclosure. Photograph courtesy of Aaron Tucker.
Figure 3-13. EPack2 (A) PCB and (B) enclosure. Photograph courtesy of Aaron Tucker.
CHAPTER 4
PHANTOM EXPERIMENTS

The redesigned EPack described in the previous chapter was tested in two phantom models. Data obtained from these models were used to verify that the design goals for EPack2 were achieved. The performance of EPack2 was compared with its predecessor in terms of precision, speed, power consumption and safety.

Experimental Models

Resistor Phantom

A resistive phantom was constructed from 16 identical resistors (100 Ω ± 5%) arranged in a network with eight external nodes and one internal node illustrated in Figure 4-1. The resistor phantom was used to evaluate the EPack’s basic performance independent of the electrode-skin interface. Data collected in this phantom were expected to achieve the best possible performance.

Figure 4-1. Schematic of resistor phantom. The resistor phantom had eight external nodes, E1 through E8, and one central node. The resistors were all 100 Ω ± 5%.
Cylindrical Saline Phantom

A cylindrical saline phantom modeling the human torso was also used to assess the performance of EPack2. The saline phantom was useful because it included a noisy electrode-electrolyte interface similar to electrode-skin contact, and tended to receive more EMI than the resistive phantom due to its larger size. The cylindrical tank was constructed from polycarbonate plastic. The tank was 450 mm high, and had a diameter of 269mm. The tank was filled with 22 liters of saline solution that had the same conductivity as an average torso, 5 Ωm (1.16g NaCl/L H₂O). Sixteen stainless steel bar electrodes were arranged equidistantly around the equator of the cylinder. Each bar electrode was 140 mm (6 in.) long, 0.5 in. wide and 0.1 in. thick. For experiments with the hemiarray, only half the electrodes were used. A photograph of the saline phantom is shown in Figure 4-2.

Methods

EPack1 and EPack2 were each used to make \( n_C = 1000 \) repeated measurements of \( \Delta Z_M \) in the resistor phantom. The resistance of the phantom was assumed to be static. Under this assumption, the signal-to-noise ratio (SNR) was given by the ratio of the measurement average and standard deviation (Cook et al. 1994)

\[
SNR = 10 \log \frac{\sum_{i=1}^{n_C} (Z_i)^2}{\sum_{i=1}^{n_C} (Z_i - \bar{Z})^2}
\]  

(4-1)

Similar measurements of the SNR were obtained from a total of \( n_C = 1000 \) repeated measurements of the saline phantom using the method described by (4-1). SNR measurements in the tank also assumed no conductivity change during the measurements.
Figure 4-2. Photograph of the cylindrical saline phantom. Photograph courtesy of Aaron Tucker.
The spatial variability of QI volume estimates of the hemiarray and full-array was compared. Blood-like anomalies with volumes ranging from 50 to 200 mL were prepared using saline-doped TX-151 gels (Walker et al. 2004). The procedure for making the TX-151 gels is detailed in Appendix A. The gels were placed at different target positions along one of three major axes in the cylindrical saline phantom. The \( \alpha \)-axis extended from the center of the tank towards its anterior, the \( \beta \)-axis was directed laterally from the center, and the \( \gamma \)-axis traveled posteriorly. Three positions in each of these axes were tested, plus the central position, for a total of ten positions as shown in Figure 4-3.

The experiment was repeated in three longitudinal positions in the tank. Anomalies were first located in the central plane (PL1). Next they were moved higher to the plane through the superior edge of the electrodes (PL2), and finally they were moved to a plane one-half-electrode
length from the superior edge of the electrodes (PL3). The three measurement planes are illustrated in Figure 4-4. In each plane, anomalies were located in one of the ten target positions along the alpha, beta or gamma directions. In total, 30 positions were tested using four anomaly volumes (50, 100, 150, 200 mL).

**Results**

The phantom experiments were used to compare the performance of the hemi-array against a similar eight-electrode full array, and to compare the first generation EPack with the redesigned variant.

![Figure 4-4. Experimental setup for measuring the longitudinal variability of QI (Sadleir et al. 2008).](image)
Electrode Array Comparison

QI was found for conductive targets with volumes ranging from 50 mL to 200 mL, located at one of 30 positions in the cylindrical saline phantom. For each target volume, the average and standard deviation of the QI estimates were calculated. QI estimates measured using the hemi- and full-arrays were compared, shown in Figure 4-5. The average QI value was found to be linearly related to the actual anomaly volume in both arrays. The square of the correlation coefficient, \( R^2 \), was 0.98 and 0.99 for the full array and hemi-array, respectively. Over the entire domain, the hemiarray and full array had a similar linearity in the QI response to volumetric conductivity changes. However, the variation in the QI over anomaly position, as measured by the standard deviation, was about five times larger in the hemiarray than in the full array. The volumetric uncertainty in the QI estimate due to spatial variation was on the order of 10 to 15 mL for the full electrode array, but was as large as 50 to 100 mL for the hemiarray. This result was expected because the hemiarray was less uniformly sensitive over all the tested positions. The level of uncertainty was still within a useful clinical range.

Figure 4-5. Comparison of the variability of the QI in (A) the eight electrode full array and in (B) the hemiarray.
Instrument Comparison

Results of phantom experiments were used to compare the first and second generation EPack devices. Comparisons were based on the aperture speed, and the precision of the devices.

Aperture speed

The amount of time necessary to capture one EIT frame was defined as the aperture time, $t_a$. A short aperture was important to reduce blurring associated with physiological processes like breathing and blood flow. For a hemi-array system with $n_E$ electrodes there were a total of $n_E$ distinct current injections pairs. For each injection, $(n_E - 3)$ voltage measurements were recorded so there were a total of $n_E(n_E - 3)$ voltage measurements per acquisition. For the EPack, $n_E = 8$, so there were 40 measurements in total. Each of these voltage measurements required a sampling period $t_{sample} = \frac{n_C}{f_0}$. Therefore the minimum theoretical acquisition time was:

$$t_{a(min)} = n_E(n_E - 3) \frac{n_C}{f_0}, \quad (4-2)$$

where $n_E$ was the number of electrodes, $f_0$ was the frequency of the current injection and $n_C$ was the number of current injection periods. EPack2 averaged over $n_C = 10$ periods, so the minimum
theoretical aperture time was about 6.5 ms operating at \( f_0 = 62.5 \text{ kHz} \). Accounting for the delay caused by multiplexer settling, \( t_{\text{mux}} \), the acquisition time was:

\[
 t_a = n_E (n_E - 3) \left( \frac{n_c}{f_0} + t_{\text{mux}} \right).
\] (4-3)

EPack2 allowed \( t_{\text{mux}} = 1 \text{ ms} \) for multiplexer settling, so the expected acquisition time was 46.4 ms.

The aperture time was deterministic, and was measured using the DSP’s internal timer. Figure 4-6 compares the aperture time in the two EPack generations. EPack2 had a measured aperture time of \( 47 \pm 1 \text{ ms} \), a major improvement over EPack1 which required \( 386 \pm 1 \text{ ms} \).

The maximum frame rate measured how quickly the EPack system can record a measurement, calculate and display the reconstruction, and then continue to the next measurement. Frame rate was important because it measured how quickly information can be made available to clinicians. Frame rate included the aperture time, the data transmission time, and the reconstruction time. The frame rate is nondeterministic and depends on the capabilities of the PC used. With a 2 GHz Pentium IV processor, 1 GB of RAM, and minimum background processes the frame rate was about 1.5 frames per second.

**Precision**

EPack2 was not only faster, but it also had better precision. The SNR results for each EPack generation were compared in Figure 4-7. The 40 transimpedance measurements are numbered across the x-axis. The SNR in EPack2 was \( 15 - 20 \text{ dB} \) higher than in EPack1.

The EPack2 performance was compared across phantom models to determine the major noise contributors. Figure 4-8 shows the breakdown of the signal and noise components in EPack2 measurements of the resistive phantom. Figure 4-8A shows the range in the signal levels for different transimpedances. A strong signal (large transimpedance) was measured when the
Figure 4-7. Comparison of the SNR on measurements of the resistor phantom using EPack 1 and EPack2. The numbering order of the measurements in the hemiarray drive pattern was illustrated in Figures 2-4 and 2-5.

transmit electrode pair is proximal to the receive pair. As the separation between transmit and receive increases the signal decreases. Figure 4-8B shows that the noise level was independent of the particular transimpedance being measured. This type of noise is voltage detector dominated (Frangi et al. 2002).

Figure 4-9 shows the breakdown of the signal and noise components in EPack2 measurements of the saline phantom. Figure 4-9A shows a similar range in the signal levels (transimpedances) in the measurement frame. Figure 4-9B illustrates how noise in the phantom, unlike in the resistor phantom, was proportional to signal level. This type of noise is current source dominated (Frangi et al. 2002). Comparing 4-8C to 4-9C we see that SNR in the saline phantom was about 20 dB lower than the SNR in the resistive phantom. A large portion of noise
was evidently attributable to the presence of electrodes, and this noise was current source dominated.

Figure 4-8. Signal and noise in the resistor phantom measured by EPack2. The dynamic range of the signal is about 4 dB while that of the noise is less than 1 dB. The correlation between the signal level and SNR is apparent. Decreasing the dynamic range of the signal will improve the SNR. The horizontal line in the SNR plot indicates the average SNR over all measurements, 58 dB.
Figure 4-9. Signal and noise in the cylindrical saline phantom measured using EPack2. Noise was correlated with the signal level. The red horizontal line in the SNR plot indicates the average SNR over all measurements, 45 dB.
CHAPTER 5
IN VIVO EXPERIMENTS

Following encouraging results from phantom experimentation, two in vivo models of IAH were tested using the EPack2 system. In vivo data were useful in evaluating the performance of existing methods, and also in the development of new reconstruction methods. Retrospective reconstructions are useful, for example, in selecting the regularization parameter.

Electrodes

Five commercially available electrodes were compared for in vivo use with the EPack. Electrodes designed for use with transcutaneous electrical nerve stimulation (TENS) were suitable due to their low cost, disposability, and large size. These electrodes have a conductive adhesive gel that helps keep them in place during monitoring. The primary drawback with TENS electrodes was that they were placed one at a time. This was time consuming, and misplacement can cause reconstruction artifacts.

The Ultima SoftTouch electrodes were used in preliminary studies with success. However, the manufacturer subsequently changed the electrode formulation to have considerably higher contact impedances. The impedance of these SoftTouch electrodes was too high and saturated the CCS. This prompted the comparison of several different brands of electrodes to select a replacement.

Elongated, rectangular electrodes from several manufacturers were tested. The five different electrodes that were tested are pictured in Figure 5-1. Metrics used to select amongst the electrodes were a) nominal impedance low enough not to saturate the CCS and b) large height-to-width ratio. Elongated electrodes improved longitudinal sensitivity as discussed in chapter two.
To compare the impedance of each candidate, two electrodes from each manufacturer were placed back-to-back. The insulation was stripped away from the safety connectors, and the back-to-back impedance was measured at 62.5 kHz using a Hewlett-Packard 4192A low frequency impedance analyzer. Each electrode was assumed identical, and the measured impedance was divided in half to obtain the approximate impedance of the electrode. It should be noted that this measured quantity was different from the electrode-skin contact impedance, but was controlled against factors external to the electrode.

The results are summarized in Table 5-1. Note that the impedance of the second batch of Ultima SoftTouch was ten times higher than the first batch, and was generally much higher than
Table 5-1. Comparison of TENS electrodes

<table>
<thead>
<tr>
<th>No.</th>
<th>Brandname</th>
<th>Dimensions (cm x cm)</th>
<th>Impedance (Ω)</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Axelgaard Platinum</td>
<td>5 x 13</td>
<td>50</td>
<td>Unstable compared to the others</td>
</tr>
<tr>
<td>2</td>
<td>Tyco Unipatch</td>
<td>5 x 10</td>
<td>42</td>
<td>Used in clinical trial</td>
</tr>
<tr>
<td>3</td>
<td>Medical Products Online</td>
<td>5 x 9</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Ultima SoftTouch 1</td>
<td>4 x 10</td>
<td>25</td>
<td>Used in preliminary studies</td>
</tr>
<tr>
<td>4</td>
<td>Ultima SoftTouch 2</td>
<td>4 x 10</td>
<td>250</td>
<td>Unusable batch</td>
</tr>
<tr>
<td>5</td>
<td>Axelgaard Platinum Blue</td>
<td>4 x 9</td>
<td>25</td>
<td>Gel is messy</td>
</tr>
</tbody>
</table>

The electrodes were carefully placed around the subject’s abdomen during in vivo experimentation. A tape measure was used to measure the subject’s girth. The appropriate electrode spacing was determined from this measurement, allowing the electrodes to be spaced equidistantly around the anterior half of the abdomen, using the iliac crests (hip bones) as a landmark for placing the first and last electrodes. The inferior edges of the electrodes were at the level of the umbilicus. Figure 5-2 is a photograph of the electrodes placed around the abdomen in the hemiarray configuration.

**Ingestion Model**

Ingestion of conductive fluid was used as a simple, convenient model the IAH. This model was non-invasive and was useful as a preliminary in vivo test of the EPack DAS and the proposed reconstruction methods.

**Methods**

Chicken flavor bouillon cubes were mixed with water in a ratio of one cube per 500 mL of water to make a solution with the approximate conductivity of blood (1.5 Ωm). The solution was kept near 37 °C to minimize temperature related impedance variation.
A volunteer fasted for 12 hours prior to the experiment. Once connected to the EPack2, the volunteer rested in a supine position for a two minute baseline. After the baseline period expired, the volunteer drank 200 mL of the soup while remaining in a supine position. It took less than a minute for the volunteer to finish the soup. The EPack continuously monitored changes in the abdominal impedance before, during and after the soup’s ingestion at a frame rate of 1 Hz.
Results

Time series of each of the 40 transimpedances are plotted in Figure 5-3. The SNR of each transimpedance was calculated from data in the baseline portion of the experiment using (4-1). The *in vivo* SNR was similar to that predicted in the cylindrical saline phantom. Figure 5-4 compares the average SNR in three modalities: resistive, saline, and *in vivo*.

**Voltage Recording Pair**

![Graph showing voltage recording pairs](image)

Figure 5-3. Time plots of each transimpedance against time in the soup model.
Figure 5-4. Comparison of the SNR measured using the EPack2 in different targets.

Figure 5-5. \( l \)-curve for an EIT measurement taken after a subject ingested soup.
Inspection of the $l$-curve was used to select a regularization parameter. Depending on the noise level in each frame, truncations ranging from $k = 10$ to $k = 16$ were indicated by the $l$-curve. Figure 5-5 shows the $l$-curve for a representative frame taken two minutes after ingestion of soup, and reconstructions of that frame using a range of regularization parameters for comparison.

The QI timeseries was calculated using regularizations in the full range between $k = 1$ and $k = 20$. The QI noise measured before ingestion of the soup was compared across each of these regularizations to determine the best $k$ value. Figure 5-6 shows the results of this comparison.

<table>
<thead>
<tr>
<th>$k$</th>
<th>Est. Mass (g)</th>
<th>Time (mins)</th>
<th>Std</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>95.6573g</td>
<td>0-15</td>
<td>0.2</td>
</tr>
<tr>
<td>7</td>
<td>95.6573g</td>
<td>0-15</td>
<td>0.3</td>
</tr>
<tr>
<td>10</td>
<td>95.6573g</td>
<td>0-15</td>
<td>0.4</td>
</tr>
<tr>
<td>14</td>
<td>95.6573g</td>
<td>0-15</td>
<td>0.5</td>
</tr>
<tr>
<td>18</td>
<td>95.6573g</td>
<td>0-15</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Figure 5-6. Comparison of QI calculated using different regularization parameters, $k$. Standard deviation (std) of 100 samples recorded before the ingestion (highlighted in red) was compared for each $k$. 

95
Overall, $k = 12$ resulted in good image reconstructions for most frames. A reconstruction sequence of the soup ingestion using this regularization is shown in Figure 5-7A. Figure 5-7B shows the same frames reconstructed with WMN. Both sets of reconstructions show typical features of EIT reconstructions, including artifacts near the electrodes, poor localization of the

![Images of reconstructions](image)

Figure 5-7. Images, mass estimate and mass flow rate estimate measured during ingestion of soup.
conductivity change, and overall diffuse resolution. Nevertheless, a distinct change was observable in the reconstructions after the soup was ingested.

The effect of breathing was evident in the QI during the baseline period. As was discussed in Chapter 2, phantom experiments predicted longitudinal sensitivity to extend above and below the electrode plane. The area of sensitivity included the lungs, and therefore pulmonary variations had a significant effect on the QI. Figure 5-8 illustrates the effect of breathing in the QI. Respiration was filtered from QI using a lowpass, 25-sample running average filter. The filtered QI is compared against the unfiltered version in Figure 5-8.

Figure 5-8. Breathing artifact in QI in ingestion model. The effect of breathing was reduced using 25-point moving average filter (bold).
Figure 5-7 shows a synopsis of the ingestion model results. The filtered QI is graphed in Figure 5-7C, showing the correspondence of reconstructed images to the QI. Figure 5-7D shows the $dQI/dt$ for soup ingestion. There was a large spike in $dQI/dt$ corresponding with the ingestion of the soup.

**Discussion**

Ingestion of soup was detectable using hemiarray reconstructions, but it was not well-localizable, nor was it well-resolved. Quantitative results were similar to those obtained using full 16-electrode arrays, validating the hemiarray configuration (Sadleir and Fox 2001).

Several complicating factors limit the strength of conclusions from the soup model. Without a control imaging method to confirm the position of the soup, the soup model functioned primarily as a test of the EPack2 instrumentation and reconstruction methods. Physiological processes associated with digestion, but not IAH, possibly confounded results of the test, e.g. secretion of gastric acid. Additionally, transimpedance measurements were likely less sensitive to soup because it was shielded by the higher resistivity of the stomach. A stronger sensitivity was expected to free conductive fluid in the abdomen, outside of abdominal organs and vasculature.

**Peritoneal Dialysis Model**

In the second *in vivo* model of IAH, patients undergoing peritoneal dialysis (PD) were monitored during a routine dialysis exchange. PD is an invasive procedure used to clear urinary waste in patients with renal failure (Maxwell *et al.* 1959). In PD, dialysate solution ($\sigma = 1.2$ S/m) is introduced into the abdomen through a surgically placed catheter, illustrated in Figure 5-9. The dialysate absorbs wastes that would normally be extracted by the kidneys, and is then drained. PD patients repeat this process regularly every 4 – 6 hours during the day. PD was a useful model of IAH because it involves controlled infusion of a conductive fluid into the abdomen.
Peritoneal dialysate was more conductive than blood. Its resistivity was 0.8 Ωm, compared to 1.4 Ωm for blood. Despite the fact that the resistivity of dialysate was about 40% less than blood’s, it was not expected to be easier to detect using EIT, because the EIT reconstruction problem is non-linear. Linearly increasing the conductivity contrast of anomalies within a background does not give a proportional change in the impedance measurements once a contrast of two or three has been reached. Less than 10% difference was expected between the transimpedances measured for conductivity between blood as compared to dialysate (Sadleir 1996).

Methods

Subjects undergoing care at the University of Florida’s nephrology clinic were recruited for the study. Patients were excluded based on their age (no minors), pregnancy or use of implanted electric devices. Five patients undergoing PD at the University of Florida’s dialysis clinic were recruited for the study. Of the five, two were excluded based on their medical history. The remaining three subjects, one male and two females, were each monitored using the EPack2
during routine dialysis exchanges. The study was conducted with the approval of the University of Florida Health Science Center’s Institutional Review Board (UF IRB-01). Informed consent was obtained from subjects prior to their participation.

Subjects underwent a peritoneal dialysis exchange while EIT data were recorded at a frame rate of 1 Hz. Subjects were responsible for dialysis bag attachment and draining. Minimal interference was made to standard PD protocols, with the exception that subjects were asked to breathe normally, lie supine and as still as possible during the procedure. Despite the subjects’ best intentions it was difficult for them to remain completely still for such a long time whilst their abdomens filled. Outliers generated by movement were documented.

At the beginning of each session, a resting period was used to obtain a baseline. This baseline was comparable to that from the soup model, and provided useful experimental information about the level of uncertainty in the recordings caused by artifacts such as breathing. After the baseline period, dialysate was allowed to flow into the abdomen under the influence of gravity. This active flow period modeled IAH.

The dialysate bag was hung from a digital hanging scale (CCi Scale Company, Inc HS-6, Ventura, CA, USA) that had a precision of ± 2 g. Figure 5-10 shows a photograph of the measurement setup. As dialysate drained into the abdomen, the mass of dialysate remaining in the bag was recorded. Serial recordings from the scale were used to determine the mass of dialysate in the abdomen. The dialysate flowed under the influence of gravity. Dialysate in the tube connecting the dialysate bag to the abdomen was assumed to be negligible, so all the dialysate drained from the bag was assumed to be dwelling in the abdomen.

The mass of dialysate in the abdomen, \( m(t) \), was used as an experimental control. The density of dialysate, and blood, are approximately 1 g/mL, therefore measurements of the mass
of dialysate are nearly identical to the volume of dialysate (Hinghofer-Szalkay and Greenleaf 1987). To avoid introducing extra variables, mass (and mass flow rate) were used in data analysis rather than volume (and volumetric flow rate).

The total mass of prescribed dialysate varied based on a patient’s medical history and physiology, but was generally 1.5 – 2 kg. After all the dialysate was administered it was allowed to dwell while a second baseline was recorded. The baseline period after administration was at least several minutes, and varied according to patient comfort. After EIT recording finished,

Figure 5-10. Measuring the mass of the dialysate. Photograph courtesy of Aaron Tucker.
subjects drained the dialysate themselves. This period was not recorded using EIT because subjects needed to move to completely drain the dialysate properly, and this would have interfered with the EIT recordings. Subjects’ blood pressure, pulse rate, and weight were also monitored for safety.

As their schedules permitted, patients returned to repeat the experiment. At least one month elapsed between successive sessions. A total of nine sessions were recorded: two with patient 1, four with patient 2, and three with patient 3. To identify patients and sessions anonymously, in accordance with the federal Health Insurance Portability and Accountability Act (HIPAA) regulations, patients were identified numerically, and sessions were labeled alphabetically. For example, 2C referred to the second patient’s third session.

The sessions were conducted as similarly as possible, with the following exceptions. A technical error during the session 1A limited the frame rate to 0.5 Hz, but was resolved in future sessions. In sessions 3B and 3C an improved scale was used to measure the mass of dialysate in the hanging bag. The scale was able to measure with a ±0.1 g precision and was also able to record measurements autonomously at a rate of 4 Hz.

**PD Reconstructions**

Reconstructed images generally had mediocre resolution and were prone to artifacts. Representative reconstructions are shown in Figure 5-11A. Pixels very near the electrodes and heavily weighted pixels in the posterior abdomen were most susceptible to noise. For \( m(t) \) smaller than about 100 g it was difficult to distinguish actual accumulations from artifacts. Beyond 200 g, dialysate was more clearly discernable. As the mass of dialysate approached 1 L the small-conductivity-change assumption was violated, and the anomaly became distorted and occupied the most of the image field. Without a control imaging modality, it is hard to interpret the significance of the images. Nonetheless, there was a clear accumulation within the region.
Figure 5-11. Time series of a single EIT session. (a) Weighted reconstructions of *in vivo* dialysate accumulation (b) Time series plot of the dialysate mass estimated using QI. Arrows indicate the times, highlighted with squares, in the QI series corresponding to the reconstructions (c) Time series plot of the actual dialysate mass as measured using a scale (d) Time series plot of the dialysate flow as estimated using dQI/dt (e) Time series plot of the actual dialysate flow interpolated from serial mass measurements. The dashed lines indicate the start and stop of fluid flow, respectively.
PD Quantification

QI and the actual dialysate mass in the abdomen, \( m(t) \), were fit to a linear model using linear regression. Results of that analysis were used to convert QI values into estimated dialysate mass,

\[
m(t) = c_1 \text{QI} + c_0
\]

where \( c_1 \) had units of \( \Omega \text{ g m} \), and \( c_0 \) was the offset correction with units of g. Data from only the first 1.8 kg of fluid injection were used to calculating the linear regression because the QI-mass linearity only holds for small conductivity change. Fits were applied to individual patients, as detailed in Table 5-2, and to all the combined set of all patients, shown in Figure 5-12.

![Figure 5-12. Regression analysis of the QI-mass relationship for nine data sets.](image)

\[\text{Fit Results:} \]
\[\text{Mass} = 47600 \times \text{QI} + 52.0 \]
\[R^2 = 0.935\]
Figure 5-13. Results monitoring impedance changes in IAH model over time. The estimated mass of dialysate compared favorably with actual mass.
Table 5-2. Quantification of dialysate mass in two patients.

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Trial</th>
<th>( c_{i} = QI/m ) (Ω m kg)</th>
<th>( R^2 )</th>
<th>stdev(QI)</th>
<th>Drift g/min</th>
<th>Girth (cm)</th>
<th>Weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A*</td>
<td>66.2</td>
<td>0.993</td>
<td>24.3</td>
<td>-8.7</td>
<td>0.618</td>
<td>81</td>
<td>46</td>
</tr>
<tr>
<td>B</td>
<td>53.0</td>
<td>0.983</td>
<td>17.0</td>
<td>6.83</td>
<td>0.341</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>47.5</td>
<td>0.991</td>
<td>21.2</td>
<td>-8.42</td>
<td>0.340</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>50.2</td>
<td>0.977</td>
<td>27.7</td>
<td>3.89</td>
<td>0.046</td>
<td>112</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>64.7</td>
<td>0.985</td>
<td>55.7</td>
<td>20.6</td>
<td>0.301</td>
<td></td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>46.8</td>
<td>0.987</td>
<td>43.1</td>
<td>-11.5</td>
<td>0.161</td>
<td></td>
</tr>
<tr>
<td>Patient 2</td>
<td>A</td>
<td>47.5</td>
<td>0.997</td>
<td>27.8</td>
<td>-17.7</td>
<td>0.867</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>38.8</td>
<td>0.995</td>
<td>39.1</td>
<td>-22.7</td>
<td>0.747</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>48.7</td>
<td>0.997</td>
<td>18.2</td>
<td>-9.03</td>
<td>0.523</td>
<td></td>
</tr>
<tr>
<td>Combined</td>
<td>-</td>
<td>47.6</td>
<td>0.935</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 5-13 compares the timeseries plots of \( m(t) \) and \( m(t) \) for each patient. The estimates strongly corresponded to the actual mass, with \( R^2 = 0.93 \) over all patients combined.

**Static analysis**

The static baseline period modeled normal, health patients. The baseline noise level of the filtered QI was analyzed by calculating the standard deviation of 300 consecutive samples recorded during the initial baseline. The noise level for each patient is listed in Table 5-2. Imprecision seemed to be inversely related to the size of the individual, as evidenced by the girth and weight of subjects in Table 5-2, but this could not be verified due to the small sample size.

300 samples of QI during the static period were fit to a linear model to measure the QI baseline drift. Table 5-2 shows the drifts for each patient. Drift tended to be negative. \( R^2 \) values for the fits, also shown in Table 5-2, were small and indicated that linear drift was non-linear.

**Dynamic analysis**

QI was shown to be well-correlated with changes in the mass of conductive solution in the abdomen; however, QI could not be used as parameter for detection of bleeding because its
offset value, $c_0$, was variable under the influence of noise, and selection of the reference measurement frame, $Z_0$. This made it hard to choose a QI threshold value for IAH detection.

QI measures net mass change but the reconstruction method is actually measuring the rate of mass change. Therefore a parameter that was related to the mass flow rate, $m'(t)$, was sought as a predictor of IAH. The slope of QI, $dQI/dt$, was such a parameter. Using $dQI/dt$ was convenient because it removed the variable offset in QI, $c_0$, but retained the important information relevant to changes in the abdominal impedance.

d$QI/dt$ was calculated from least-squares linear regression of $d = 60$ samples of QI. At a frame rate of 1 Hz, a total of 60 s were required to collect this amount of data. For each session, 100 sequential $dQI/dt$ values were measured from the resting baseline, and compared against 100 sequential $dQI/dt$ values measured during active dialysate infusion. The estimated mass flow rate was:

$$m'(t) = c_1 \frac{dQI}{dt}$$

Figure 5-11 shows results for the complete algorithm for one patient. Figure 5-11A shows reconstructions using WMN at several time points. Figure 5-11B shows the timeseries plot of $m(t)$. Arrows illustrate the correspondence of the reconstructed images to the mass time series, and vertical dashed lines indicate the start and stop of dialysate flow. The estimate closely followed $m(t)$, which is plotted in Figure 5-11C. The estimated mass flow rate, $m'(t)$, is shown in Figure 5-11D and was compared to the $m'(t)$ time series in Figure 5-8E.

The optimum threshold for IAH detection was determined using the receiver operator characteristic (ROC) curve (Metz 1978). ROC analysis tested whether $dQI/dt$ could be used to distinguish between baseline periods and active infusion. An equal number of points were
selected for each period to avoid skewing the results. Figure 5-14 shows a histogram that compares mass estimates obtained using $dQI/dt$ in baseline periods and active infusion.

The ROC curve showed the tradeoff in sensitivity and specificity as the threshold was varied. Sensitivity was defined to be the true-positive rate (TPR) and specificity was equal to the compliment of the false-positive rate (1 - FPR). For each possible threshold level, the TPR and FPR were calculated and plotted on the ROC curve, shown in Figure 5-15.

![Histogram of dQI for Non-Bleeding Patients](image1)

![Histogram of dQI for Bleeding Patients](image2)

**Figure 5-14.** Distribution of estimated mass flow rates in positive and negative models of IAH.
The area under the ROC curve, which indicates the quality of the test, was 0.997. This indicated \( \frac{dQI}{dt} \) was an excellent discriminator between the static and active models. The \( p \)-value for the test was less than \( 1 \times 10^{-6} \).

The optimum threshold was defined to be the point closest to \( TPR = 1 \) and \( FPR = 0 \) on the ROC curve. This choice of threshold assumed the cost of false-positives was equal to the cost of false-negatives. Irrespective of the particular method of threshold selection, the ROC curve shows the prediction value for all possible detection thresholds.

Figure 5-15. ROC curve for the detection of IAH.
Table 5-3. Confusion matrix for detection of modeled IAH using a threshold of 60 mL/min.

<table>
<thead>
<tr>
<th>ACTUAL</th>
<th>PREDICTED</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>883</td>
<td>17</td>
<td>900</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>43</td>
<td>857</td>
<td>900</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>926</td>
<td>874</td>
<td>1800</td>
<td></td>
</tr>
</tbody>
</table>

The optimum threshold was 60.6 mL/min. At this threshold the sensitivity was 98% and the specificity was 95%. The full confusion matrix for this threshold value is shown in Table 5-3.

Discussion

Quantitative EIT methods like those examined in this study de-emphasize the use of reconstructions for localization. Instead, relevant information about the subject’s condition is extracted from the reconstructions, which are themselves only intermediate results. The results of this study are significant because they were collected from a sub-optimal hemi-array of electrodes, and because they are the first human in vivo data confirming previous simulated and phantom studies with the hemiarray (Sadleir et al. 2008). The QI and dQI estimators were robust to in vivo noise levels, which will be inevitable in some environments despite efforts to eliminate instrumentation noise.

Our results suggest that a hemorrhage rate of 60 mL/min should be detectable in vivo using this EIT method. While we expect that the sensitivity of EIT to dialysate in the abdomen should be slightly higher than its sensitivity to blood, we believe a value around threshold would probably also be observed for blood. Because both fluids have large conductivity contrasts relative to background abdominal tissue, the measurement response to presence of a volume of either fluid will be ‘saturated’ in each case (Seagar, Barber and Brown 1987). This is supported by previous studies performed measuring quantitative sensitivity of a related method to volumes.
of blood-like fluid in an abdominal phantom (Sadleir and Fox 1998) and dialysate in the abdomen in vivo (Sadleir and Fox 2001), where we found very similar sensitivities in both cases.

Measures similar to QI can be obtained from a single transimpedance. This bioimpedance approach involves fewer electrodes and does not require solving an inverse problem. But, the EIT approach gives a more uniform sensitivity than is measured from a single transimpedance, and affords some redundancy, allowing clinicians to identify technical problems influencing the QI and dQI data, e.g. misapplied electrodes. At best, the images might be clinically useful for distinguishing between haemorrhages on the left or right sides of the abdomen, but further improvements to image quality are hampered by uncertainty in the boundary shape, due to both anthropomorphic and temporal variation.

The speed of accurate diagnosis is critical in the treatment of traumatic injuries. These results show that the rate of bleeding can be measured using EIT in less than 60 seconds after electrode application, less than half the imaging time required for a trained operator to complete a FAST diagnosis using ultrasound (Thomas et al. 1997). Not only is EIT potentially faster, but it requires less attention from the operator who is freed to attend other responsibilities once the device is applied.

Variations on the methods used herein can reduce the variability in QI, and are expected to improve dQI. One such possibility is defining a region of interest so as to ignore troublesome pixels near the boundary (Meeson 1995). A weighted reconstruction technique designed to minimize QI variability was also proposed, based on normalization of the power spread function (Oh et al. 2009). That reconstruction technique typically halved the variability of phantom reconstructions.
The specificity of this method is likely affected by other physiological processes. In this study we observed that EIT was sensitive to movement, breathing and digestion. Further, the effect of traumatic injury on bioimpedance is not well understood. The physiological reaction to trauma may mask or exaggerate impedance changes caused by blood accumulation. Changes in body temperature will also affect the bioimpedance. Careful study of these challenges is important to the advancement of this technology.

The results presented here are of course preliminary; due to the small sample size it would be premature to draw statistical conclusions based on this data. Nevertheless, the results do illustrate the proof of concept and allow us to fine-tune our methods in preparation for larger clinical trials.
CHAPTER 6
EPACK3

Introduction

The next generation device for IAH detection, EPack3, will be integrated on an electrode belt designed to simplify application of the electrodes, and to guarantee their accurate positioning. The belt will be constructed from flexible PCB (FlexPCB) with silver electrodes (0.5 inch x 3 inch) immersed onto a copper substrate. The surface of the electrodes will be chemically converted to Ag/AgCl by application of household chlorine bleach (NaClO). Nonconducting surfaces of the belt are coated in polyimide laminate.

Improvements in the EPack instrumentation were proposed based on the phantom and in vivo results, in preparation of more extensive clinical trials with the EPack3 integrated belt. A prototype system with an entirely redesigned digital subsystem, and substantial revision of the analog subsystem was designed. The digital and analog subsystems were designed separately, with a modular connector to allow independent development of the subsystems. Figure 6-1 shows the EPack3 prototype system diagram. Testing of the prototype design was further simplified by neglecting the analog multiplexer, and using only four electrodes to test the DAS.

Analog System Redesign

EPack3 was designed to operate at any frequency on the band 1 kHz – 100 kHz, but it was optimized for operation at 50 kHz. EPack2 was optimized for operation at 62.5 kHz to accommodate its particular digital architecture limitations, but EPack3 was designed without those limitations. 50 kHz was near enough to 62.5 kHz to have little effect on the results.
Figure 6-1. EPack3 system overview
**DDS Noise Reduction**

Noise in the DDS made a significant contribution to the overall system error because it was the first component in the signal chain. Figure 6-2 illustrates noise in the EPack2 DDS. Spurious fee dynamic range (SFDR) was less than 30 dBc, and the noise floor is no lower than -60 dBc.

The DDS was reconfigured to take advantage of the fully-differential output on the AD9850 integrated circuit. This reduced the effect of noise in two ways. First, differential signaling made the DDS output less susceptible to common mode EMI. Second, differential signaling doubled the effective signal swing compared to similarly powered single-ended lines.
An active filter was designed to condition the DDS output before it arrived at the Howland source. The filter served three purposes. First, the DC component of the DDS output was blocked using ac-coupling. The DC offset was significant because the DDS operated on a single +3.3 V supply. Without the DC block, the offset would be multiplied by the DC transconductance of the current source and cause a hazardous DC output current.

The second function of the filter was to attenuate quantization noise, spurious harmonics, and clock noise in the DDS output spectrum. This was achieved using a first order low-pass filter (LPF) with the corner frequency set to the operating frequency. To offset the -3dB attenuation caused by the LPF at the operating frequency, the midband gain of the filter was set to about 3dB.

Finally, the filter served as a low impedance source used to drive the inputs of the Howland. As discussed previously, the source impedance can cause mismatch in the Howland circuitry. The bandpass filter also was required to have a low noise figure and low distortion to prevent corruption of the voltage reference.

The filter topology is illustrated in Figure 6-3. Because the filter formed part of the load for the DDS, the input impedance had to be set carefully. The input impedance of the filter was required to be 200 Ω so the DDS would see a total equivalent load of 100 Ω and operate within its voltage compliance limits. The midband input impedance of the filter was $R_1 || R_2$, so this was set to 200 Ω.

$C_{in}$, $R_1$, and $R_2$ formed a high-pass filter that blocks DC. The cutoff frequency for this high-pass filter was

$$f_H = \frac{1}{2\pi(R_1 || R_2)C_{in}}.$$  \hspace{1cm} (6-1)

Using (6-1), $C_{in}$ was set to 800 nF to set the high-pass cutoff at 1 kHz.
The DC bias was reset to zero by $R_1$, which provided a ground return for the opamp input bias current. Because $R_1$ was fairly small, the opamp input bias current which did not create a large DC offset.

The midband voltage gain of the filter is

$$A_v = -\frac{R_3}{R_2}.$$  \hfill (6-2)

$R_3$ was chosen to be 300 $\Omega$ so the gain would be 1.5 V/V or about 3.5 dB. $R_3$ and $C_F$ form a low-pass filter with a corner frequency at:

$$f_L = \frac{1}{2\pi R_3 C_F}.$$  \hfill (6-3)

Setting the lowpass corner frequency at 50 kHz required using a 10nF capacitor for $C_F$. 

---

Figure 6-3. Bandpass filter for preconditioning the voltage reference to the current source.
The Analog Devices ADA4898 opamp was selected based on its low output impedance (0.1 ohm), low voltage noise density (1 nV/rtHz), and low distortion (HD2 < -100 dBc).

The filter was simulated in LTspice using the manufacturer-provided model for the ADA4898. Figure 6-4 shows the magnitude of the filter transfer function, |H| = |Vout / Vin|. There was -20dB/decade attenuation outside the filter passband. The passband was not flat; however, because we operate at one operating frequency this is not an important limitation.

The output-referred noise, $e_n$, is plotted in Figure 6-5. There was significant 1/f noise contributed by the opamp, but at 50 kHz the output-referred noise was $e_n = 117$ nV/rtHz, which was sufficiently low.

![Figure 6-4. Bandpass filter transfer function.](image-url)
Current Source

EPack3 featured an improved Howland current source that had 80 dB of precision while operating at EIT frequencies. In this section, the theory, design, simulation and testing of the new current source are detailed.

The improved Howland, shown in Figure 6-6, is a popular version of the basic Howland current pump that has wide output swing and low power consumption (Franco 2002). The improved Howland has better performance, but it is more complicated to analyze than the original Howland.

The Howland is unique and interesting because it has both positive and negative feedback paths. The feedback paths are balanced when the resistors are matched according to

\[
\frac{R_4}{R_3} = \frac{R_{2A} + R_{2B}}{R_1}.
\]

With its feedback paths in ideal balance, the Howland was modeled as a linear voltage-controlled current source (VCCS), as shown in Figure 6-7. The model was driven by an external, independent voltage source (not shown) that drove the VCCS input. The transconductance, \(G_m\).
Figure 6-6. Improved Howland current source.

![Improved Howland Model](image)

**Improved Howland Model**

\[
Z_O = R_{O1} \parallel R_{O2} \parallel (-j\omega C_0)^{-1}
\]

Figure 6-7. Linear model of the improved Howland current source. The output impedance, \(Z_O\), is a stray path that diverts output current away from the load, and limits the precision of the current source.
converted the input voltage, $v_{IN}$, into an output current, $i_{OUT}$. The output current’s dependence on the load, $Z_L$, was modeled by the output impedance, $Z_O$.

**Input considerations**

The Howland has a fully differential input under the ideal condition that (6-4) is satisfied perfectly. However, the positive and negative inputs have different transconductances when that condition is not perfect, and therefore it is better to drive only one input and ground the other to avoid unnecessary distortion. The positive and negative transconductances, $G_m^{(+)}$ and $G_m^{(-)}$, of the improved Howland are

$$G_m^{(+)} = \frac{i_{OUT}}{v_{IN^+}} = \frac{R_{2A} + R_{2B}}{R_1 \cdot R_{2B}}. \quad (6-5)$$

$$G_m^{(-)} = \frac{i_{OUT}}{v_{IN^-}} = \frac{R_3}{R_3 \cdot R_{2B}}. \quad (6-6)$$

The positive input was used so the Howland’s input and output are in phase, but the design issues discussed henceforth are independent of input selection.

The voltage source driving the Howland must be carefully considered as a separate design issue. The source impedance should be kept as small as possible because it is in series with either $R_1$ or $R_3$ (depending on selection of positive or negative input) and can cause equation (6-4) to become unbalanced. The source voltage should be as large as practical to reduce the effect of interference.

**Output compliance**

The maximum output voltage magnitude, $|v_L|$, is:
\[ |v_L| \leq |v_{\text{SAT}}| - \frac{R_{2A} + R_{2B}}{R_t} |v_{IN}|. \]  

(6-7)

where \( |v_{\text{SAT}}| \) is the saturation voltage of the opamp (Franco 2002). For EIT, it is intuitive to assume a constant current and consider the output compliance in terms of the maximum load, \( R_L^{\text{max}} \), i.e.,

\[ R_L^{\text{max}} = \frac{|v_L|}{|v_{\text{OUT}}|}. \]  

(6-8)

Combining (6-5), (6-7), and (6-8) yields a useful expression for the maximum load,

\[ R_L^{\text{max}} = \frac{|v_{\text{SAT}}|}{|v_{\text{OUT}}|} - R_{2B}. \]  

(6-9)

**Noise**

Accounting for Johnson thermal noise, and the opamp equivalent input-referred noise voltage density, \( e_n \), the output-referred noise current density is

\[
  i_n^{(\text{out})} = 4k_B T \sqrt{\frac{(R_{2A} + R_{2B})^2}{R_t R_{2B}^2} + \frac{R_4^2}{R_t R_{2B}^2} + \frac{R_{2A} + R_{2B} + R_4}{R_{2B}^2} + e_n^2 \left( \frac{R_1 + R_2}{R_1 R_{2B}} \right)^2}. 
\]  

(6-10)

where \( k_B \) is Boltzmann’s constant \((1.38 \times 10^{-23} \text{ J/K})\) and \( T \) is the absolute temperature. When operating at EIT frequencies we can generally neglect 1/f noise. The opamp equivalent input-referred current noise can also be neglected unless very large resistors are used in the Howland.

**Output impedance**

The precision of the EIT measurement depends on the output impedance of the current source, \( Z_O \). \( Z_O \) limits the precision of the delivered current. For an application requiring \( b \) bits of precision in the magnitude of the current, \( Z_O \) must satisfy
\[
\frac{Z_O}{Z_O + Z_L^{\text{max}}} - \frac{Z_O}{Z_O + Z_L^{\text{min}}} \leq \frac{1}{2^b},
\]
where \(Z_L^{\text{max}}\) and \(Z_L^{\text{min}}\) are the maximum and minimum loads anticipated (Saulnier 2005). If the load is always much smaller than the output impedance, then the requirement is approximately

\[
Z_O \geq 2^b (Z_L^{\text{max}} - Z_L^{\text{min}}).
\]

Three independent factors contribute to the output impedance, \(Z_O(\omega)\).

\[
Z_O(\omega) = R_{O1} \parallel R_{O2} \parallel \frac{j}{\omega C_O}.
\]

A model combining their effects is presented in Figure 6-7. The first of these factors is related to the balancing of the positive and negative feedback paths. The feedback paths are balanced when the resistors are matched according to (6-4). Realistically there will be some error, \(\varepsilon\), in the matching:

\[
\frac{R_1}{R_3} = \frac{R_{2A} + R_{2B}}{R_1} (1 - \varepsilon).
\]

The finite output resistance resulting from feedback mismatch is

\[
R_{O1} = \frac{R_{2B} (R_1 + R_{2A})}{\varepsilon \cdot (R_{2A} + R_{2B})}.
\]

\(R_{O1}\) was maximized by using high precision (expensive) resistors, analog (Pease 2008) and digital (Oh, Woo and Holder 2007) trimming schemes, careful PCB design (Rafiei-Naeini and McCann 2008), and remembering that the resistance of the source driving the Howland is in series with \(R_1\) or \(R_3\).

The matching error, \(\varepsilon\), should not be confused with the tolerance, \(\text{tol}\), of the resistors. If a nominal resistance, \(R\), with tolerance, \(\text{tol}\), was used for all four resistors in (6-4), and the worst-case mismatch scenario was assumed, then (6-4) can be written

123
\[
\frac{R(1+\text{tol})}{R(1-\text{tol})} = \frac{R(1-\text{tol})}{R(1+\text{tol})}(1-\varepsilon). \tag{6-16}
\]

For small tolerances this simplified to
\[
\varepsilon = 4 \cdot \text{tol}. \tag{6-17}
\]

The opamp’s finite open-loop gain, \(A_{OL}\), was the second factor that limited precision. The effect of finite \(A_{OL}\) was determined using loop gain analysis (Gray et al. 2009). The negative feedback path around the opamp, consisting of the resistors \(R_3\) and \(R_4\), formed a standard non-inverting amplifier. \(T^-\) is the loop gain around that loop:
\[
T^- = A_{OL} \frac{R_3}{R_3 + R_4}. \tag{6-18}
\]

With the negative feedback path closed, the non-inverting amplifier has closed loop voltage gain, \(A_V\), given by:
\[
A_V = \frac{(1 + R_4/R_3)}{1 + 1/T^-}. \tag{6-19}
\]

The second loop, the positive feedback, is composed of the (closed loop) non-inverting amplifier, \(R_1\), \(R_{2A}\) and \(R_{2B}\). The loop gain around the second loop, and indeed for the entire system, is then
\[
T^+ = A_V \frac{R_1}{R_1 + R_2}. \tag{6-20}
\]

The load is connected in shunt to the positive feedback loop, thus the closed loop output resistance (Hurst 1992), \(R_{O2}\), is given by
\[
R_{O2} = \frac{R_{OL}}{1 - T^+}. \tag{6-21}
\]

where \(R_{OL}\) is the open-loop output resistance given by
\[
R_{OL} = (R_1 + R_{2A}) || R_{2B}. \tag{6-22}
\]
Combining (6-4), (6-19) and (6-20), the system loop gain becomes

\[ T^+ = \frac{1}{1+1/T^-}. \]  

Equation (6-23) shows the unique property of the Howland, that the shunt feedback in the positive feedback loop looks like series feedback in the negative feedback loop. As a result, \( T^+ \) must be maximized to obtain a large \( R_{O2} \).

Combining (6-18)–(6-22), and assuming (6-4), the output resistance resulting from finite opamp \( A_{OL} \) is given by

\[ R_{O2} = \left( (R_1 + R_{2A}) \parallel R_{2B} \right) \left[ 1 + A_{OL} \frac{R_3}{R_3 + R_4} \right]. \]

(6-24)

The above equation assumes perfect matching of the feedback paths, since any mismatch is accounted for independently in \( R_{O1} \).

The final limitation on the Howland’s output impedance is the finite gain bandwidth of the opamp. This consideration is particularly important for applications operating around 10 kHz or faster. At high frequencies, the opamp open-loop gain is diminished. This is modeled using a first order system

\[ A_{OL}(s) = \frac{A_{OL}}{1 + p_1/s}. \]  

(6-25)

where \( A_{OL} \) is the DC open loop gain of the opamp, and \( p_1 \) is the dominant pole given by:

\[ p_1 = \frac{f_H}{A_{OL}}. \]

(6-26)

This pole impairs the performance of the feedback system at high speeds, causing \( R_{O2} \) to roll off at -20 dB/decade at frequencies above \( p_1 \) (Gray et al. 2009). It is important to have enough bandwidth to support a large \( A_{OL} \); otherwise, \( p_1 \) may be below the operating frequency. The roll-off is modeled by output capacitance, \( C_O \), given by
\[
C_O = \frac{R_1 + R_4}{2\pi f_H R_3 \left[ (R_1 + R_{2A}) \| R_{2B} \right]}.
\]

(6-27)

This equation for the output capacitance is similar to an over-simplified one given by Steele and Green (1992), which assumed \( R_{2B} \ll (R_1 + R_{2A}) \) and resulted in a 33\% error for our Howland configuration. It is also different than a formula for \( C_O \) given by Pease (2008), which appears to be incorrect by our analysis.

**Component selection**

80 dB of precision is equivalent to 14 bits, and in our application the load varies by as much as 200 \( \Omega \). According to (6-12), the minimum output impedance is about 3.3 M\( \Omega \). To meet this precision requirement, and to realize the necessary transconductance, noise level, output impedance, and voltage swing, we set \( R_1 = R_3 = R_4 = 2 \text{ k}\Omega \) and \( R_{2A} = R_{2B} = 1 \text{ k}\Omega \). This sets \( G_m^{(+)} = 1 \text{ mA/V} \) and \( R_{L_{\text{max}}} = 2.3 \text{ k}\Omega \), and gives a large value for the loop gain, according to the second term in (6-24).

To maximize \( R_{O1} \), resistors with 0.01\% tolerance were used. According to (6-15) and (6-17), \( R_{O1} \) was 3.75 M\( \Omega \). This was very close to the minimum \( Z_O \) requirement of 3.3 M\( \Omega \). While we could have used trimming to further improve matching, this would have introduced lengthy calibration procedures, stray capacitance, and additional hardware that would unnecessarily complicate the design. Therefore the opamp was selected very carefully so as not to degrade the output impedance further.

\( R_{O2} \) could be effectively neglected if it were much larger than \( R_{O1} \). This required \( A_{OL} \) of at least 94dB according to (6-24). Next, to ensure \( C_O \) was sufficiently small for operation at 50 kHz, \( f_{\text{H}} \) of at least 2.2 GHz was specified by (6-26). An opamp that met these requirements was the Texas Instruments OPA847 (\( A_{OL} = 98\text{dB}, f_{\text{H}} = 3.9\text{GHz}, \epsilon_n = 0.85 \text{nV/rtHz} \)). Using the OPA847,
we expected $R_{O2} = 29.7 \, \text{M}\Omega$, $C_O = 0.11 \, \text{pF}$, and $i_n^{\text{(out)}} = 11.8 \, \text{pA/rtHz}$ according to (6-24), (6-27) and (6-10), respectively.

High speed opamps can cause instability in Howland circuits (Hong et al. 2009). In our case, the OPA847 has minimal internal compensation, making it very prone to instability A compensation scheme that improves stability without degrading output impedance was necessary.

**Input capacitance compensation**

A common source of instability is parasitic capacitance at the opamp’s input terminals. This capacitance is usually at least 1-2 pF. Ross et al. (2003), Franco (2002), Rafiei-Naeini and McCann (2008), and Pease (2008) indicate that placement of a feedback capacitor, $C_F$, in parallel with $R_4$ as shown in Figure 6-8, is appropriate for compensation. This is an effective strategy, provided that $C_F$ is related to the inverting input’s parasitic capacitance, $C_{PN}$, according to:

$$C_F = C_{PN} \left( \frac{R_3}{R_4} \right).$$

(6-28)

When $C_F$ is not matched exactly, the wideband output impedance will be degraded because (6-4) will become unbalanced at high frequencies. An error as small as 1 pF can reduce the bandwidth by a decade or more. Satisfying (6-28) is difficult when $C_{IN}$ is not known with accuracy, or if tightly-toleranced capacitors are unavailable or expensive. Moreover, in our case, this compensation is ineffective because the source of instability is an internal opamp node, rather than the input terminal.

**Load compensation**

A similarly unsuitable compensation technique in this context would have been the use of a series RC ‘snubber’ network in parallel with the load (Steele and Green 1992). This technique is effective for stabilizing a Howland with an inductive load, an uncommon situation in
biomedical applications, whose loads are usually capacitive. Motor control applications are one example of an application where a current source would see an inductive load (Steele and Green 1992).

**Lead-lag compensation**

Lead-lag compensation was an effective compensation technique, and was implemented using a series R-C network between the input terminals, as illustrated in Figure 6-9.

The compensated loop gain was found using the extra element theorem (Middlebrook 1989) and is given by

\[
T_{\text{stable}} = T^* \cdot \left( \frac{1 + sR_eC_c}{1 + s(R_d + R_e)C_c} \right).
\]

where \( T^* \) is given by (6-23), and \( R_d \) is given by:
Lead-lag compensation added a zero at \( f_z = \left( \frac{2\pi R C}{C} \right)^{-1} \) and a pole at \( f_p = \left[ \frac{2\pi (R_d + R_C) C}{C} \right]^{-1} \) to the loop gain. This compensation technique was effective because it reduced high frequency loop gain and reduced the phase delay near the unity gain frequency. The pole, which attenuated the loop gain, was set just above the desired operating frequency so as not to reduce the closed-loop output impedance at operating frequencies according to (6-4). The pole frequency, \( p_C \), was set by \( C_C \). Since \( R_d \gg R_C, R_C \) had little effect on the pole frequency. The zero reduced the phase shift, and is adjusted by setting \( R_C \) to give maximum phase margin for a given \( C_C \).

The stability of the circuit was simulated using LTspice (Engelhardt 2011) using the manufacturer-provided opamp model for the OPA847, which includes the relevant opamp non-idealities. The worst-case resistor mismatch was simulated assuming 0.01% tolerance resistors. The loop gain was simulated using the test fixture bundled with LTspice (Tian et al. 2001). The
simulated loop gain was used to measure the phase margin. Transient analysis was used to confirm the stability indicated by the phase margin. LTspice was also used to plot the output impedance against frequency in order verify that the output impedance was high enough.

**Construction**

The circuit was carefully constructed on a four-layer printed circuit board using surface-mount 0603 resistors with 0.01% precision. Symmetrical layout was used to achieve excellent matching. Short traces ensured that the trace resistance was much smaller than the resistor tolerances. Ground plane was removed beneath the opamp input terminals to minimize parasitic capacitance. Figure 6-10 shows the EPack3 analog subsystem PCB.
Results and discussion

Figure 6-11 shows the magnitude and phase of the loop gains with and without lead-lag compensation from simulation. The plot has been drawn to make it easy to visually estimate the phase margin. For the uncompensated case, the unity gain frequency is near 300 MHz, but at that frequency the phase has already exceeded $-180^\circ$. The uncompensated system therefore doesn’t have positive phase margin, and is unstable.

Lead-lag compensation improved the system’s stability. The best results were obtained by setting $C_C = 250$ pF and $R_C = 58$ Ω, yielding a stable phase margin of $63^\circ$. Figure 6-12 shows the

![Figure 6-11](image)

Figure 6-11. Loop gain plot of compensated and uncompensated Howland current sources using the OPA847 opamp. The plot has been drawn to make it easy to visually determine the phase margin by first determining the unity gain frequency from the magnitude plot, and then determining the phase at the unity gain frequency from the phase plot.
resulting wideband output impedance of our Howland source, which was 3.3 MΩ up to 200 kHz. The -3 dB frequency of the output impedance was 455 kHz. The precision met our requirement, and the bandwidth exceeded our design specification.

The resistor tolerances are the limiting factor for the Howland’s output impedance, but we have shown that excellent precision is achievable despite this constraint when the opamp is selected carefully. Using 0.005% resistors, simulation predicts the same design would have 5.8 MΩ output resistance. This option would expensive, but more affordable and faster to construct than custom integrated circuits.

Figure 6-12. Output impedance of lead-lag compensated, improved Howland current source. The simulation included the effects of worst-case resistor mismatch and realistic opamp model provided by the manufacturer. The output impedance was 3.3 MΩ and the -3 dB frequency was 455 kHz.
Lead-lag compensation was an effective strategy for stabilizing the Howland because it did not sacrifice the high frequency output impedance. Unlike other compensation techniques, lead-lag compensation can be used to significantly increase the phase margin for any unstable Howland circuit.

Designing a system for measuring the output impedance of the Howland source is as complex as designing the current source itself. The ‘droop’ method is the most accurate method of measuring the output impedance of the current source (Cook 1994). The droop method uses a current-controlled voltage source (CCVS) with variable input impedance, which is the load seen by the Howland. The CCVS converts the output current into a buffered voltage that is measured using an ac voltmeter, thus isolating the Howland from the voltmeter’s input impedance. By varying the input impedance of the CCVS, the change in the CCVS output voltage can be related to the output impedance of the current source; however, the accuracy of the measurement is limited by the accuracy to which the input impedance of the CCVS is known, the accuracy of the CCVS gain, and the accuracy and noise level of the voltmeter measuring the CCVS output. It is actually quite easy to exaggerate the output impedance by lack of attention to these details, which is not uncommon in some literature on the Howland. Therefore, claims of ultra-high output impedance (e.g., $Z_0 = 10 \, \text{M}\Omega$) should be verified against the theoretical limitations presented here.

Applications requiring higher precision must resort to calibration circuitry and procedures to trim out resistive mismatch. Calibrated Howland sources must be adjusted frequently, because miscalibration will degrade performance severely, certainly worse than the design presented here. For those applications, Pease gives a good trimming procedure that can be automated (2008); however, this procedure does not involve direct measurement of the output impedance.
For EIT, having achieved 80 dB of precision in the current source is sufficient because there are other sources of error, both in instrumentation and in reconstruction, that introduce considerably more uncertainty.

**Variable Gain Amplifier**

Another improvement was the re-introduction of variable amplification in the voltmeter. This feature was included in the EPack1, but never implemented in software. EPack2 removed this feature because of limited availability of GPIO that was instead used to control the crosspoint switches. The revised EPack3 architecture had the necessary GPIO to control a programmable gain amplifier, and a simple, automated gain control routine was designed in software.

Variable gain control is important because of the wide range of the abdominal transfer impedances. The small transimpedances result in very small signals through the voltmeter that are vulnerable to noise corruption. These noisy measurements have a deleterious effect on the reconstructions, which are heavily influenced by noise due to the ill-conditioning of the inverse problem. Applying gain to the small measurements was expected to boost the SNR of the small measurements, and reduce noise artifacts in the reconstructions.

The Analog Devices AD8253 was selected to replace the AD620 used in EPack2. This instrumentation amplifier has very high CMRR at EIT frequencies. The amplifier’s gain was controlled via a 2-bit digital interface that allowed the gain to be set from 1 to 1000 in decade increments. Settling time of the gain setting was negligible compared to the multiplexer settling time.

The gain was set using a software automated gain control (AGC) routine. The first step of the AGC was measuring each transimpedance using a gain of one. After obtaining all the measurements, the DSP was able to determine the maximum amount of gain that could be
applied to each measurement without saturating the voltmeter. The gain profile was stored in memory and used for subsequent measurements. Subsequent measurements were measured using the stored gain settings. In the event of large increases in the transfer impedances, saturated measurements were detected using the overflow output on the ADC, and the gain for those measurements was decremented.

**Digital System Redesign**

A major feature of the EPack3 was a completely redesigned digital subsystem that took advantage of two decades of advances in DSP technology since the original EPack was designed. Major advantages of the redesign included faster operation, larger available memory, lower power consumption, better debugging capabilities and a smaller overall footprint. Most importantly, the redesign gave EPack3 the power to process data in real-time using advanced digital algorithms that were not possible on EPack2.

**DSP**

The core of the digital redesign was an upgrade from the Analog Devices ADSP2181 to Texas Instruments TMS320F28335 Delfino DSP. Relevant improvements that this DSP included were:

- Operation at 125 MHz
- Support for 32-bit floating-point arithmetic
- Low voltage operation (3.3V I/O, 1.8V Core)
- Integrated, electrically erasable and programmable read-only memory (EEPROM)
- Multiple, independent pulse-width modulation (PWM) modules for clock generation
- Real-time debugging via joint test action group (JTAG) interface.
- Integrated universal asynchronous receiver transmitter (UART)
- Two programmable, external interrupt pins
- 50 general purpose input or output (GPIO) pins
- External direct memory access (DMA) interface to receive 16-bit ADC results
- Freely available C language compiler
Digital Clock Signals

The DSP was clocked by the FOX924B TCXO oscillator operating at 25 MHz. The FOX924B had excellent frequency stability of ± 2.5 ppm, which was important because the DSP is used for generating low-jitter clocks for the DDS and ADC. The oscillator was a very low power device, drawing only 6 mA at 3.3 V. It also had a very small footprint, only occupying 16 mm² of PCB space.

The DSP had an internal phase-locked loop (PLL) that multiplied the input clock up to the maximum clock speed, 125 MHz.

The DDS and ADC clock signals were generated by the DSP using the pulse width modulator (PWM) peripheral.

Power

The DSP was powered by the Texas Instruments TPS70531, a low dropout voltage regulator. The regulator converted a 5 V input voltage into dual 1.8 V and 3.3 V rails required by the DSP. The regulator also had built in reset control and reset supervisor to ensure proper booting when the system was powered on or reset. The voltage regulator package had improved heat dissipation using an exposed pad on the bottom of the package to sink heat into the PCB.

Communications

EPack3 had a maximum baud rate of 1Mbps, about ten times faster than EPack2. This was accomplished by using a faster digital isolator (ISO7221C), and improved PCB layout with shortened data lines.

The integrated serial communications interface (SCI) on the DSP replaced several components in EPack2, including the external 16C550 UART, oscillator, and associated passive components. To further reduce space, EPack3 used the USB micro-B type connector for USB communication.
Printed Circuit Board and Construction

EPack3 was designed on a four-layer printed circuit board (PCB) that was designed using Altium Designer (Altium Ltd., Sydney, Australia) and fabricated by Advanced Circuits (Aurora, CO). Unused GPIO pins were terminated to ground with through 10 kΩ series resistance, and set as outputs to prevent damage to those pins and underlying peripherals.

DSP Code Design and Testing

The DDS was programmed in C using the Texas Instruments Code Composer development environment. The code was debugged on a PC using Code Composer’s simulator and real-time debugger via the JTAG interface. The XDS-100 programmer was used as a JTAG to USB interface to the PC. Using Texas Instruments’ Code Composer software, the JTAG interface was used to flash code onto the digital signal processor, step through the code and view internal memory using real-time emulation. The final code was stored in internal, nonvolatile flash memory.

On bootup, the DSP’s registers and peripherals were initialized. The general purpose input output (GPIO) multiplexer registers were set to determine the peripheral that has control of each of the GPIOs. GPIO pins could be used as inputs, outputs, pulse width modulator outputs, or serial communication inputs or outputs. One of the DSP’s eight 32-bit timers generated an interrupt every 0.5 ms, used for real-time (slow) timing, including runtime counter, indicator LED flashing, and monitoring of communications timeouts.

The SCI peripheral of the digital signal processor was setup to allow for both transmit and receive interrupts to the DSP. Data were transmitted and received into memory using the respective interrupt service routines. The SCI interface was programmed to operate at 921600 bps, transmitting eight data bits and one stop bit, without a parity bit. This SCI section of code supports simple configuration of the SCI UART peripheral using the PC user interface. This
code supports multiple baud rates, data lengths, stop bits and parity types. The first-in, first-out (FIFO) buffer was enabled to allow high-speed communication without losing data.

The direct memory access (DMA) module of the DSP was initialized to point to a dedicated section of RAM reserved for ADC data. The DMA was triggered by a dedicated, external interrupt pin, driven by the ADC clock. The DMA was set to allow a fixed-length burst of data and then terminate automatically.

Once the ADC data were in memory from the DMA, the DSP pre-processed the data, and transmitted it to the PC. EPack3 used a phase-sensitive detection algorithm, designed to exploit the narrow transmit bandwidth to reject most noise. Since the frequency of the transmitted current is known a priori, the detection should be insensitive to perturbations outside this narrow frequency band. Examples of out-of-band noise sources include power lines (60 Hz), fluorescent lights (1 kHz), and physiologic bioelectric signals (< 100 Hz).

**Phase sensitive detector**

The phase sensitive detector (PSD) is a useful method of extracting signals with known frequency content from high levels of noise (Blair and Sydenham 1975; Smith et al. 1992). As its name implies, the PSD is able to measure the real (resistive) and imaginary (reactive) parts of impedance independently. For the detection of IAH, only the real component is required. The PSD is frequency selective, which is why this technique is also sometimes called a lock-in amplifier (Murphy and Rolfe 1988).

The frequency selectivity of the PSD gives it several advantages over the RMS method used in EPack2. PSD is a narrowband estimate that is immune to out-of-band interference associated with thermal noise, internal system clocks, power lines and other EMI. The RMS method sums power over a wideband and therefore tends to overestimate the signal in the presence of any noise EMI source.
The EPack3 PSD multiplied the input waveform by a reference (demodulating) sinusoid whose frequency was the same as the operating frequency, \( f_0 \). The demodulating sinusoid was defined as having zero phase. The product of the reference and the input signal were found according to the trigonometric half-angle identity:

\[
A \cos^2(2\pi f_0 t) = \frac{A}{2} [1 + \cos(4\pi f_0 t)]
\]

(6-31)

The multiplication demodulated the signal, shifting half of the signal energy down to DC and the other half of the energy to a high frequency, as illustrated in Figure 6-13. Noise energy outside the narrowband signal was translated according to the trigonometric sum and difference formula:

\[
A \cos(2\pi f_0 t) \cos(2\pi f_c t) = \frac{A}{2} \cos[2\pi (f_0 + f_c) t] + \frac{A}{2} \cos[2\pi (f_0 - f_c) t]
\]

(6-32)

All noise energy outside of the operating frequency was shifted to non-DC frequencies.

Figure 6-13. Frequency content (A) before, and (B) after the demodulation step of the PSD.
The DC component was then extracted using a low pass filter (LPF), and this result was used as the estimate of the signal amplitude. The PSD algorithm is illustrated in Figure 6-14. The PSD can be implemented using analog (Blair and Sydenham 1975; Meade 1983) or digital (Yang et al. 2006) methods. Digital demodulation was preferred because the multiplication and LPF do not add noise, unlike analog demodulation. The signal voltage applied to the inputs to the analog-to-digital converter was

\[ v_{ADC}(t) = 2Z_L I_0 A_{preamp} A_{inamp} \cos(2\pi f_O t) \quad 0 \leq t < \frac{n_s}{f_O} \]  

(6-33)

This voltage was sampled by the ADC, resulting in the digital input waveform:

\[ x_{ADC}(n) = \left( \frac{2^n - 1}{V_{ADC\text{MAX}}} \right) \cdot v_{ADC}(t)_{t=n/f_s} + 2^{(n-1)} \quad n = \{0,1,2,...,n_s \cdot n_s\} \]  

(6-34)

where \( n_s \) was the ratio of the ADC sampling frequency, \( f_s \), to the injection frequency, \( f_O \):

\[ n_s = \frac{f_s}{f_O}. \]  

(6-35)

This ratio \( n_s \) was the number of samples in one cycle of the injection waveform. The input waveform is encoded as unsigned integers and there is therefore a DC offset in the digital waveform. The input waveform is multiplied by each of the demodulating signals, \( y \),

Figure 6-14. Flowchart of the PSD algorithm. The input signal is \( x(n) \) and the demodulating signal is \( y(n) \).
\[ \bar{y}_1 = y_1(n) = A_{\text{mod}} \cos \left( \frac{2\pi n}{n_y} \right) + A_{\text{mod}} \]
\[ \bar{y}_2 = y_2(n) = A_{\text{mod}} \sin \left( \frac{2\pi n}{n_y} \right) + A_{\text{mod}} \]  

(6-36)

Once again, the offset was required because we are coding using unsigned integers. \( A_{\text{mod}} \) was maximized to give the best precision in the PSD estimate. The demodulating waveform, \( y_1 \), was precalculated and stored in ROM memory. The demodulating waveform was multiplied by the input waveform, according to

\[ x \cdot y = \sum_{n=1}^{n_y} x(n)y(n). \]  

(6-37)

The product waveform was low-pass filtered using a simple average filter. This was accomplished by dividing by the total number of samples, \( n_y \). The real and imaginary components of the transimpedance were then recovered by converting the demodulating product to account for amplifier gain, DC offsets, and the analog-to-digital conversion. The real and imaginary components of the transimpedance were:

\[ \text{real}(Z_L) = \frac{\left[ \frac{x \cdot y_1}{n_y} - A_{\text{mod}} \cdot 2^{(n_y-1)} \right] V_{\text{ADCMAX}}}{A_{\text{mod}}A_{\text{preamp}}A_{\text{mump}}I_0 (2^{n_y-1})} \]  

(6-38)

\[ \text{imag}(Z_L) = \frac{\left[ \frac{x \cdot y_2}{n_y} - A_{\text{mod}} \cdot 2^{(n_y-1)} \right] V_{\text{ADCMAX}}}{A_{\text{mod}}A_{\text{preamp}}A_{\text{mump}}I_0 (2^{n_y-1})} \]  

(6-39)
CHAPTER 7
SUMMARY AND CONCLUSIONS

In the detection and treatment of IAH, every moment is critical. In this study, a new device and method for the rapid detection of IAH was proposed and tested. The EPack was envisioned to be complementary to existing methods of detecting IAH, due to its portability, low cost, and ease of use. Results obtained in this study suggest IAH accumulating faster than 60 mL/min can be detected with 98% sensitivity and 95% specificity in one minute, during which time medical personal would be free to continue concurrent diagnoses and treatments.

The EPack used an EIT methodology validated for the first time in this study. The methodology was unique because it used a subset of the electrodes ordinarily used in abdominal or thoracic EIT. Electrodes were placed only around the anterior abdomen, on anatomy that is accessible in an immobile, supine patient. Restricting the location of electrodes posed theoretical challenges for the reconstruction of EIT data, but was advantageous to the pragmatic application of this technology.

Two versions of the EPack device were designed in this study. The EPack2 was used to collect data from phantom and in vivo models of IAH. The device was reliable and safe, and was useful in verifying the IAH detection algorithm. From those experiments, it was determined that QI, and its derivative, $dQI/dt$, were useful quantitative estimators of the abdominal impedance change characteristic of IAH.

From the results obtained in those models, improvements in the EPack device were proposed, simulated, designed and tested in the laboratory benchtop. The next generation EPack3 device has an entirely redesigned digital subsystem, a high precision current source, and redesigned voltmeter and phase sensitive detector, all designed to improve measurement precision.
Eight electrode quantitative EIT techniques can be used in other applications as well. For example, an eight electrode array for the detection of intra-ventricular hemorrhage in neonates has been designed and is fully compatible with the EPack3 (Tang 2010). The array is shown in Figure 7-1.

Additional studies using the EPack3 on a wider population will be required before this technology can be used in actual trauma patients. PD is the best model at present for IAH in this modality, and efforts should be made to increase the recruitment of PD patients for additional clinical studies. Recruitment of PD patients is difficult due to their often complicated medical histories and bureaucratic obstacles to human clinical trials. Generally, PD patients have been interested in participation in the study, based on their interest in new technology, and
compensation that was offered. However, independent outpatient dialysis centers have been
reluctant to participate with this study due to perceived lack of benefits for the dialysis centers,
risks associated with changes to their normal operations, and increased overhead in preparing for
the study. Cooperation with clinical personnel will be the critical limiting factor in recruitment
for further studies.

The PD model of IAH should be revised in future studies to allow controlled variation of
the dialysate flow rate. An infusion pump can be used to control the flow rate. Many PD patients
are using some sort of infusion pump at home; however, one was not available for use in the
clinical trial. This methodology would give a better indication of EIT’s sensitivity to different
flow rates. Ultimately, the ability to distinguish different hemorrhage rates will be of interest to
trauma clinicians.
APPENDIX
PROCEDURE FOR MAKING TX-151 BLOOD EQUIVALENT ANOMALY

TX-151 blood equivalent anomaly has a conductivity of 0.67 S/m and can be produced following this procedure.

1. Prepare the amounts of each ingredient following Table A-1.

2. Combine ingredients in a glass beaker and stir thoroughly using a glass stirrer (a handful of glass stirrers may be useful as the solution thickens).

3. Cover the solution using plastic film. Poke some holes in the film to allow ventilation.

4. Microwave for 9 minutes (may vary with microwave). The solution is overheated if it begins bubbling or boiling. Allow about one minute of cooling before proceeding.

5. Carefully pour the hot mixture into the mold. Avoid mixing in air.

6. Cover the mold with plastic film and refrigerate for 4 hours. The anomaly is ready once it has solidified.

7. Wrap unused anomalies with plastic wrap and keep refrigerated.

Table A-1. Composition of blood equivalent anomaly

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Purpose</th>
<th>Mass (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deionized Water</td>
<td>Principal Ingredient</td>
<td>492</td>
</tr>
<tr>
<td>Sucrose</td>
<td>Sets electric permittivity</td>
<td>84</td>
</tr>
<tr>
<td>Agar</td>
<td>Solidifier</td>
<td>15</td>
</tr>
<tr>
<td>TX-151</td>
<td>Thickener</td>
<td>15</td>
</tr>
<tr>
<td>Sodium Chloride</td>
<td>Sets electric conductivity</td>
<td>3</td>
</tr>
</tbody>
</table>
LIST OF REFERENCES


Bertemes-Filho P 2002 Tissue characterization using an impedance spectroscopy probe. PhD dissertation, Department of Medical Physics and Clinical Psychology, University of Sheffield, Sheffield, UK.


Boone K G and Holder D S 1996 Current approaches to analogue instrumentation design in electrical impedance tomography Physiol. Meas. 17 229–47.


Branney S W, Moore E E, Cantrill S V, Burch J M and Terry S J 1997 Ultrasound based key clinical pathway reduces the use of hospital resources for the evaluation of blunt abdominal trauma *J. Trauma* 42 1086–90.


Clarke J R, Tooskin S Z, Doshi P J, Greenwald L and Mode C J 2002 Time to laparotomy for intra-abdominal bleeding from trauma does affect survival for delays up to 90 minutes *J. Trauma* 52 420–5.


Frerichs I 2000 Electrical impedance tomography (EIT) in applications related to lung and ventilation: a review of experimental and clinical activities Physiol. Meas. 21 R1–21


IEC60601-1 2005 Medical Electrical Equipment Part1: General Requirements for Basic Safety and Essential Performance (Brussels: International Electrotechnical Commission)


Oh S 2009 "Compensation of shape change artifacts and spatially-variant image reconstruction problems in electrical impedance tomography," PhD dissertation, Department of Biomedical Engineering, University of Florida, Gainesville, FL.


Sadleir R J 1996 “Electrical impedance tomography applied to the detection of intra-peritoneal bleeding,” PhD dissertation, Department of Physics and Department of Electrical and Electronic Engineering, University of Western Australia, Crawley, WA.


Shackford S R, Rogers F B, Osler T M, Trabulsy M E, Clauss D W and Vane D W 1999 Focused abdominal sonogram for trauma: the learning curve of nonradiologist clinicians in detecting hemoperitoneum *J. Trauma* 46 553–64.


Tang T 2010 "Detection of neonatal intraventricular hemorrhage with electrical impedance tomography." PhD dissertation, Department of Biomedical Engineering, University of Florida, Gainesville, FL.


BIOGRAPHICAL SKETCH

Aaron S. Tucker was born in Chicago, IL in the early 1980s. When he was young, his family moved to South Florida. In 2002, he graduated from the International Baccalaureate (IB) program, completing the nation’s most exigent high school program with specialties in psychology, European history, Spanish language, and English literature, and earning highest marks in mathematics and physics. In 2002, he was also awarded the prestigious National Merit award.

He received the B.S. degree in electrical and computer engineering and the M.S. degree in biomedical engineering from the University of Florida, Gainesville, FL in 2006 and 2009, respectively. As an undergraduate student, he concentrated on designing small autonomous robots and custom digital electronic systems. He was on the UF Presidents’ Honor roll several times. Later, as a graduate student his focus shifted to mixed-signal embedded electronics useful for medical diagnostics. He has also designed data acquisition systems for studies of psychological olfactory reception.