# Effect of Angulus on Patient-elevation Compliance

12/13/2016

**SPECIFIC AIMS**

Ventilator-associated events (VAE) are the scourge of critical care settings and hospital systems at large. There is extensive evidence that ventilator-associated pneumonia (VAP) and related VAEs increase mortality rates in critically ill patients by up to 50%[1,2], while simultaneously increasing cost of care[3]. Collectively, VAP and other VAEs result in extended hospital stays[2], additional ventilator time, and reactionary treatment approaches. This translates into a tremendous cost burden for hospitals and compromised clinical outcomes.

Best-practice guidelines state that positioning ventilated patients at an angle between 30-45 degrees significantly reduces the potential for VAP and other VAE to develop[11,12,13,14]. While the intent of the guidelines is to govern **patient elevation angle**, the lack of a mechanism to accurately measure patient elevation requires that nurses rely on the **head-of-bed (HOB)** protractor – a tool which reflects the angle of the bed, not the patient - to measure compliance. **Depending upon the position and posture of the patient in the bed, a patient's elevation angle may be significantly different from the HOB angle. Critical care teams currently rely on built-in HOB protractors and digital inclinometers that measure the angle of the bed not the patient.** The inability to effectively, accurately and reliably measure a patient's angle significantly hinders adherence to and effectiveness of HOB guidelines[5,6] and the larger "VAP bundle" – a set of evidence-based standards published by the CDC shown to significantly reduce incidences of ventilator-associated pneumonia.

Angulus, LLC has developed a dual-component Angulus sensor to fill this gap in critical care technology. Angulus enables critical care practitioners to instantaneously understand a patient's elevation, identify when the patient is outside of the desired 30-45 degree recumbency scope, and efficiently correct the patient's orientation with immediate feedback. Angulus supports real-time minute-to-minute data display as well as longitudinal aggregation of data. It objectively measures a patient's elevation, provides alerts when patients are out of range, and allows users to query for instant data and aggregate trends. With Angulus, critical care teams can effortlessly view a patient's elevation angle at-a-glance, eliminating the need for burdensome and inexact HOB measurement tools. Further, the ability to collect real time continuous patient elevation data may provide the necessary longitudinal data to further refine and improve patient elevation guidelines.

**We seek to empower critical care teams to increase adherence to the VAP-prevention bundle, and thereby improve patient outcomes in the intensive care unit**. Enabling critical care treatment teams to view comprehensible on-demand data about a patient's real-time elevation will empower greater compliance to the VAP prevention practices, and thereby reduce the incidence of VAP and other VAEs.

**To achieve our overarching goal, we will pursue the following four specific aims:**

1. **Conduct initial end-user focus groups with critical care teams and stakeholders at our evaluation site**. In order to validate existing HOB-adherence pain points and determine which critical hardware and software features end-users find most essential, we will conduct focus groups with the critical care team at our evaluation site, Montefiore Medical Center.
2. **Measure the effect of Angulus on patient-elevation (HOB) compliance**. To validate the usefulness of Angulus in improving compliance with patient elevation, and to elucidate the usability and feasibility of Angulus, we will conduct a randomized crossover study implementing Angulus within two ICU's at our evaluation site, Montefiore. This study will allow us to determine the effect of the Angulus mechanism on compliance, and quantify the percentage of time patients are spending within the desired recumbency with Angulus, when compared to the current standard of care.
3. **Integrate critical end-user functionality post- implementation with an agile and iterative product development approach and assess end-user satisfaction and usability scores.** Feedback from end users post implementation will enable us to enter a product refinement stage. We will measure satisfaction and usability outcomes, and gather feedback on user experience design and integration workflow hurdles. Collectively, this data will enable us to guide our next stage of product development.

By the completion of this grant, we will have tested the Angulus prototype and made significant progress toward developing Angulus 2.0. Completion of these aims will enable Angulus to conduct a larger scale efficacy trial with Phase II funding, and will position the company to pursue commercialization efforts accordingly.

**Significance**

The goal of this application is to empower critical care teams to increase compliance with evidence-based patient elevation guidelines through the implementation, evaluation and refinement of Angulus – a novel dual-

component system for measuring a patient's elevation angle in real time. **There is currently no available technology for critical care teams to measure patient elevation. Present methodologies measure the angle of the bed, are typically primitive, and fail to have the alerting and data gathering capabilities required to implement true compliance.**

Ventilator-associated pneumonia (VAP) refers to pneumonia that develops at least 48 hours after the initiation of mechanical ventilation.[1,2] VAP is considered to be a hospital-acquired infection (HAI) with incidence rates ranging between 10-65%[1,2,18,19,20]. VAP has a 30% mortality rate[1,2,3,18] and results in an extended hospitalization – on average patients with VAP stay an additional 4.3 days in the ICU[1,2,3,4]. Hospitals incur an additional $40,000 in incremental costs per patient[3], and nationally, our healthcare system is spending $10 Billion a year on reactionary VAP treatment strategies. The data shows that VAP translates into profound cost expenditures and significantly compromised clinical outcomes for care settings. Adverse patient outcomes, in addition to national patient safety mandates, have made reducing or preventing the occurrence of VAP and related ventilator-associated events (VAE) a major focus of several hospital ICUs[11]. One such initiative reflecting this prioritization was the Institute for Healthcare Improvement's (IHI) nationwide effort to reduce mortality and morbidity associated with hospital care by recruiting healthcare institutions to implement measures to prevent VAP through implementation of evidence-based practices[16].

To date, several randomized trials and observational studies have been conducted to better understand the causes, risk factors, interventions and treatments for VAP[16,17,18,19,20]. As a result of these efforts, the CDC has outlined best-practice evidence-based guidelines that, with effective implementation and diligent compliance, have been shown to reduce the incidences of VAP[8]. Collectively, these guidelines are referred to as the "VAP Bundle" and patient elevation is one component of this bundle. **Given the lack of a capability to measure patient elevation, Head of Bed (HOB) angle is often used interchangeably with patient elevation. However, these are two unique measurements – a fact that has profound implications for the compliance with the VAP bundle.**

Elevation of the patient is an integral part of the VAP bundle, and has been correlated with a reduction in the rates of VAP[12,13,15]. A study published in *The Lancet* found that placing ventilated ICU patients in a semi-recumbent position between 30-45 degrees reduced the risk of VAP by 78%[17]. Yet, despite a national priority to reduce the incidence of VAP and related VAE, and a well-documented evidence base, which suggests that positioning ventilated patients at an angle between 30-45 degrees significantly reduces the potential for VAP to develop, many providers find it difficult to implement and comply with patient elevation guidelines[6,7]. A baseline assessment of ICU Nursing measures at Roxborough Memorial Hospital showed that compliance with patient elevation was low[16]. In fact, a study conducted at 33 academic medical ICUs found 60% of patients had at least one 24 hours period during which the HOB goal was never documented[6]. Compromised compliance with patient elevation does not signal an educational failure, or a lack of understanding[5], but rather it is a result of ineffective measurement tools and nonexistent signaling mechanisms for easily, accurately and efficiently measuring a patient's elevation. It is also likely that there erroneous assumption that HOB angle is equivalent to patient elevation results in a 'set it and forget it' mentality.

*Preliminary Phase I Focus Group Data*

In a preliminary focus group conducted with 20 full time ICU nurses at NY Presbyterian Hospital, 88% of nurses rated the bed angle of a ventilated patient as "very important" according to best practice guidelines. Similarly, when asked how important the bed angle of a ventilated patient is *in practice*, 76% of respondents rated it as "very important." Zero focus group respondents rated the importance of HOB angle as "moderately important," "of little importance," or "not at all important," suggesting that there is a deep-rooted understanding of the functional importance of maintaining patients at an appropriate elevation.

Existing methodologies for measuring a patient's elevation have failed to keep pace with the evolving needs and constantly increasing demands of ICU nurses[6]. Built in head of bed (HOB) protractors and digital inclinometers are the two presently available (and leading) methods for evaluating a patient's HOB angle, however these devices fail to accurately measure the patient's true elevation, and do not integrate into central ICU monitors or - at a minimum - have any mechanism for displaying data. **Preliminary focus group data showed that 47% of survey respondents did not believe the HOB protractor to be correct**, and many reported as an addendum, that HOB protractors are often broken or illegible. Without easily accessible and intelligible data from high-fidelity tools, ensuring compliance guidelines becomes quite challenging.

The HOB protractor is a particularly ineffective tool due to its limited correlation with patient elevation. This device, when not broken, is affixed to the joint in the hospital bed and functions like a grade school protractor. It measures the angle of the top half of the hospital bed relative to the bottom half of a hospital bed. Consider

for a moment, the situation in which a patient slides down the bed or contorts their orientation to achieve greater comfort. As soon as the patient has introduced these or some other individual level differences in their orientation, the HOB protractor reading is no longer an accurate reflection of the *patient* angle**. The HOB protractor measures the angle of the bed, NOT the patient.** Focus group respondents bolstered this notion as well. Nurses reported that patients sliding down the bed, adjusting themselves, or being adjusted by loved ones are the three most common events which occur frequently (every 2-3 hours) and cause patients to become misaligned, negating the value of the HOB protractor. **These frequent changes is patient position/posture necessitate a continuous monitoring strategy vs. a spot check approach to compliance.**

Current tools lack any form of a signaling mechanism, which means nurses must manually check the head of bed protractor every time they wish to attempt measure a patient's elevation. Given the difficulty inherent in incorporating this tedious and time-intensive task into their workflow[6], nurses often implement their own strategies for evaluating patient angle – including "eyeballing the patient's orientation in the bed" – the primary strategy for checking on a patient's elevation as reported by 30% of focus group nurses.

Unfortunately, despite the fact that nurses fully comprehend the critical nature of patient elevation guidelines, many believe that they do not have a high-fidelity means for accurately determining a patient's elevation, are often relying on non-functional components and piecemeal strategies, and result to hodge-podge DIY approaches for measuring the patient's elevation. If one cannot easily measure a patient's elevation, then one cannot ensure compliance with patient elevation guidelines. These archaic, error-prone, inefficient tools and approaches make the implementation of and compliance with best practice guidelines nearly impossible.

***Solution – Angulus, an eloquent system for measuring a patient's elevation and ensuring compliance***

ICUs would be better served **by agile, accurate, precise and accessible tools for measuring and signaling patient elevation angles, in real time**. Angulus was developed to fill this gap in critical care technology. Angulus is a novel unobtrusive system, which simplifies the process of measuring a patient's elevation angle in real time, and facilitates direct access and interpretation of novel measurements. Angulus accurately measures patient elevation (vs. HOB) - irrespective of a patient's idiosyncratic orientation – and transmits on-demand minute-to-minute data to a corresponding display device via low-energy Bluetooth. It also has the capability to collect and recall historical data and present longitudinal, aggregate trends. Angulus is composed of two components - a wireless sensor which is affixed to the patient's sternum via a hypoallergenic adhesive, and a corresponding software interface, which displays the patient elevation angle. (Figures 2&3)

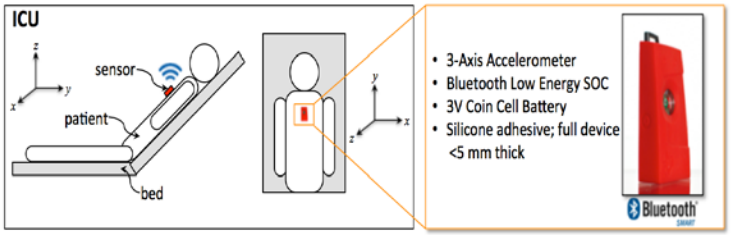



*Figure 2: Illustration of Angulus Hardware Component*


Figure 3: Examples of the UX software interface that displays patient elevation data in a graded color coded fashion

The core of the Angulus device is a SensorTag CC2650 (http://www.ti.com/tool/cc2650stk). The SensorTag incorporates several sensors: light, microphone, compass, magnetometer, hygrometer, pressure, accelerometer, gyroscope, IR thermometer, and ambient thermometer. The most relevant for us (and the only ones we use) are the 3D accelerometer and 3D gyroscope. A single chip provides "9-axis" output; the InvenSense MPU-9250 measures 3D acceleration, 3D rotation and 3D magnetic field all in one chip. This provides the platform for sub-degree accuracy. As with any application utilizing accelerometer and gyroscope-based measurements, it is possible for the output values to "drift" over time, which directly affects the accuracy of the measurement. The sources of this drift are known (ambient temperature changes, poorly chosen sampling rate), as are several techniques for fixing such drift (e.g. bias-offset calibration, using ambient temperature as input, gyro-accelerometer fusion with a Kalman filter). Like many modern sensors the SensorTag CC2650 incorporates some drift correction. In our testing, we have not observed any drift of angle readings over multi-day periods.

The Angulus Sensor enables critical care treatment teams to instantaneously evaluate a patient's airway angle, identify when the patient is outside of the desired 30-45 degree recumbency scope, and efficiently correct the patient's orientation with immediate feedback. Providers receive color coded escalating visual cues when

patients fall outside of a desired range, and can call upon user-friendly functionality such as the ability to snooze the device as needed. The Angulus sensor enables critical care teams to effortlessly view a patient's angle at-a-glance, eliminating the need for burdensome and inexact HOB measurement tools. Via the accurate measurement and delivery of on-demand data about patient elevation, treatment teams will be well positioned to better understand patient elevation, and improve compliance to best-practice guidelines.

By offering cutting edge functionality, Angulus is geared toward tackling the multi-faceted problems associated with existing ineffective methods for measuring and complying with best practice head of bed guidelines.

In this Phase I proposal we will collaborate with Albert Einstein/Montefiore Medical center to: 1) collect end user feedback from focus groups and interviews 2) conduct a randomized cross over trial to measure the impact of Angulus on improving compliance with patient elevation guidelines, 3) quantify the relational discrepancy between Angulus-generated data and HOB Protractor readings, and 4) assess end-user satisfaction and usability measures and integrate critical high value features via an agile, iterative product development life cycle. Upon achieving these aims, we will have provided critical care teams with the tools that they need to better deliver the best care possible for ventilated patients in the ICU.

By empowering critical care teams with intelligible, accessible and accurate on-demand data about a patient's elevation angle in real time, Angulus will improve compliance with patient elevation guidelines. This work will have a tremendous impact on resolving a burdensome problem associated with increased patient morbidity and astronomical costs.

**Innovation**

Currently, there is no available technology to accurately measure patient elevation and thus compliance with VAP bundle protocols cannot be assured. The Angulus device (currently in prototype form) is the first and only device that have been developed to accurately measure patient elevation angle. It is inherently unique and discrete from existing present-day techniques that measuring an intubated patient's HOB angle. It incorporates the following novel features, which are not presently available with existing technologies/approaches which measure HOB: 1) Angulus measures patient orientation objectively in 3D; no other device on the market does this, 2) the corresponding software component incorporates signal processing tools to filter erroneous measurements and minimize the false positive alert rate, 3) the device records longitudinal data on patient orientation and guideline compliance.

**Table 1.** Comparison of HOB Protractor features
**Key**: ✓= feature supported ✗= Not supported ? = To Be Determined

| Feature | HOB PROTRACTOR | ANGULUS |
|---|---|---|
| Non-Fixed (Flexible) Position | ✗ | ✓ |
| HIPAA-compliant | ✓ | ✓ |
| Accurately Measures the Patient in the Bed | ✗ | ✓ |
| Has the ability to collect and store continuous data | ✗ | ✓ |
| Supports aggregate trends data | ✗ | ✓ |
| Transmits data wirelessly | ✗ | ✓ |
| Incorporates a Software Display Screen on or near the ICU monitor | ✗ | ✓ |
| Enables users to set a custom acceptable range | ✗ | ✓ |
| **(AIM 1) Incorporates high-value end-user features (i.e. a snooze button)** | ✗ | ✓ |
| **(AIM 2) Validated Patient Angle Accuracy** | ✗ | ? |
| **( AIM 3) Improves Compliance with Patient Elevation** | ✗ | ? |
| **AIM 4) Has Favorable Usability and Satisfaction Scores** | ✗ | ? |

The Angulus device is an innovative application of existing technologies to solve an unmet medical need that has the potential to significant decrease mortality and medical costs in ICUs. The device combines proprietary software interface with accelerometer, gyroscope, and inclinometer to create a powerful tool for ensuring patient elevation compliance.

Our proposed solution is innovative in two key ways: 1) it greatly improves the approach and methodology by which providers can measure patient elevation, access those measurements and comply with best-practice guidelines; and 2) it represents a theoretical shift in that it measures the patient – idiosyncratic orientations and all - and not the bed. The dominant method for measuring patient elevation at present is the HOB protractor, and yet the HOB protractor presents significant complications to measuring patient elevation and improving compliance with patient elevation guidelines.

Our product represents a significant breakthrough in how ventilated patient orientation is managed, and the Angulus system represents a tremendous advancement in how at-risk patients are evaluated and protected from the complications of ventilation. Perhaps, most significantly, the Angulus device's ability to collect real time continuous patient elevation data may provide the necessary longitudinal data to further refine and improve patient elevation guidelines.

This product meets a significant unmet need in critical care, and given the commercial potential is favorable. This potential could be much greater if CMS ultimately adds VAP to the list of non-reimbursable hospital acquired infections as it has considered doing. Completing these aims will immediately bolster our commercialization potential in several ways. First, robust baseline data will enable us to quantify what

compliance looks like currently, and understand the potential for improvement. Understanding this relationship will allow us to understand the potential impact and effect of improving patient elevation compliance – from both an economical point of view, and an outcomes perspective. Second, understanding what end user features and functionality are considered most critical within institutions and between institutions will inform our product development process. Collecting satisfaction and usability scores via widely accepted and validated mechanisms will allow us to quantify this critical end-user feedback as well. Lastly the implementation of Angulus will allow our company to serve critical care settings with tools that improve their efficiency and compliance. This has a tremendous trickle-down impact potential for care settings. Given that the Angulus system is a non-significant risk device, we do not believe that the FDA regulatory pathway to commercialization presents tremendous hurdles or barriers.

The Angulus technology is protected by US Patent Application No. 14/675,105, and Intl Patent Application No. PCT/US15/23697, which are scheduled for publication in September of 2015. The patents being prosecuted cover both system and method for a number of monitoring metrics, with careful consideration of prior art. The IP covers the specific embodiment planned for testing as well as additional embodiments centered around other indications. The patent covers measurement of patient angle with a freestanding device. This unique IP is a significant strength over bed-mounted devices. The Angulus device monitors the patient posture, not the bed angle. Thus, the data collected from our device are a truer reflection of the patient's risks arising from body angle position. Angulus filed its first provisional application in March 2014 and its non-provisional and PCT application in March 2015. A thorough landscape search has been conducted and Angulus has freedom to operate in focus indications. One of the company's founding members, Jason Bourgeois, practices IP law. Angulus is also being supported by one of the top life science-focused IP law firms in the country — Wilson, Sonsini, Goodrich, & Rosati.

This project represents a unique and widely under-utilized collaboration between healthcare technology and academic medicine. Together, the Angulus leadership, in conjunction with our collaborative consortium agreement with Dr. Michelle Gong and Montefiore Medical Center, is uniquely suited to bring this product directly to the healthcare workers and patients who need it most.

**Approach:**

**Aim 1: Conduct initial end-user focus groups with critical care teams and stakeholders at our evaluation site, Montefiore Medical Center.**

We intend to collect data from the clinical staff from within the Intensive Care Unit (ICU) at Montefiore Medical Center to elucidate attitudes, beliefs and challenges toward head of bed compliance. Understand the unique compliance and adherence challenges that are present for providers at Montefiore. We will begin this proposal by first conducting pre-implementation focus groups with the clinical staff from within the Intensive Care Unit (ICU) at our evaluation site, Montefiore Medical Center. Any care provider or administrator responsible for the care of patients in the ICU or for quality control of the hospital outcomes such as VAP will be eligible for the surveys and focus groups. Individual surveys and focus groups will be deployed to validate the problem with HOB compliance, assess treatment providers' understanding of the VAP bundle and its importance, and understand existing challenges to measuring the patient's head of bed. We have conducted similar focus groups at New York Presbyterian Hospital, (See preliminary Phase I focus group data above), however we will gather more robust data from additional end users through a rigorous quantitative and qualitative survey and data collection process in order to understand the landscape of unique challenges that are present at Montefiore.

Additionally, for the first month of the project, we will engage our collaborators in systematic requirements gathering through stakeholder interviews conducted once a week for four weeks. At each interview the Principal Investigator and the study coordinator will interview an individual with significant experience in critical care. Interviews will cover a quantitative ranking of proposed features, and a qualitative open-ended opportunity to suggest new functionality. Utilizing this data, in conjunction with our preliminary focus group feedback from NYP, we will be able to identify common end-user needs and design inputs that exist between care settings to guide a product development strategy with the maximum potential value for multiple institutions. We will initially translate focus group data into a technical feature list. The PI will then filter and prioritize features for incorporation into the device. High value features will be implemented and tested in an alpha version of hardware and software

**Aim 2: Measure the effect of Angulus on patient-elevation (HOB) compliance**

Angulus will work collaboratively with our consortium-site PI, Dr. Michelle Gong, at our evaluation site, Montefiore Medical Center, to implement a cluster randomized crossover trial of Angulus in human subjects.

The purpose of this trial is to determine how implementation of Angulus impacts compliance with patient elevation guidelines. *Our hypothesis is that real time feedback to nurses and bedside clinician from the Angulus sensor of the actual body angle of elevation of the patient rather than the angle of the bed can improve compliance to head elevation to 30 degrees in mechanically ventilated patients in the ICU.* In order to achieve this goal we will conduct a cluster randomized crossover study occurring in two (2) Intensive Care Units (ICU) at Montefiore Medical Center. Randomization will occur at the ICU level.

Study Population: To participate in this study a patient must meet all of the inclusion criteria and fail to meet any of the exclusion criteria.

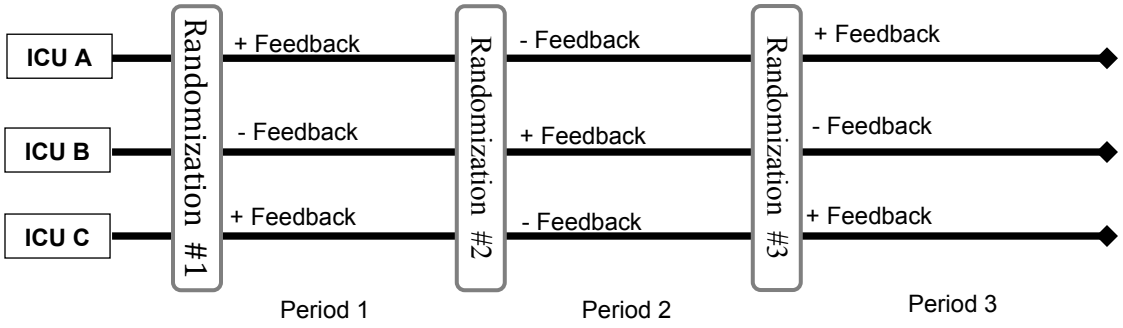
The criteria for inclusion in this study are:

- Mechanical ventilation with any modality (e.g., endotracheal tube, tracheostomy)
- Age between 18 and 75 years

The criteria for exclusion from this study are:

- Patients with a known allergy to the encasing materials
- Patients who are advised to be positioned outside of the 30-45 degree scope.
- Patients with any major chest wall abnormalities, or defects, including but not limited to:
    - post-cardiac surgical patients
    - pectus excavatum (or any congenital chest wall deformity)
    - complicated skin and soft tissue infections on the chest wall
    - heart-lung machine systems

Study Design: This is a two arm, clustered randomized cross over trial looking to see whether feedback from the Angulus device will promote greater compliance to patient elevation in the ICU. The overall study design is see in Figure 4.




After receiving full IRB approval, all ICU nurses will receive didactic training on VAP, the importance of head-of-bed elevation, and a refresher on best-practice guidelines for implementing and ensuring compliance with the VAP bundle. These trainings will take place on two (2) separate occasions before each period to ensure that all ICU nurses receive the training, and will incorporate an evaluation component to assess comprehension. During each period, research coordinator will screen each unit for newly intubated patients who fulfill the inclusion criteria but none of the exclusion criteria. Eligible patients in the study ICUs at all periods will be equipped with the Angulus Device by tape to their sternum. Each potential participant will be given a de-identified patient code. Subjects will be enrolled in the trial within 36 hours of intubation, and will remain in the trial until discharge from the ICU. *Note that the Angulus is placed externally on the patient's chest and secured with adhesives similar to what is used for EKG leads used clinically in the ICU. Angulus' only function is to measure the angle of elevation of the patient in their current position.* For further discussion on the protection of human subjects, please see the human subjects section. The Angulus device will be collecting data on patient elevation "in the background." This will allow us to quantify the extent to which compliance with patient elevation is compromised under existing workflow limitations.

During Period 1, each ICU will be randomized to Feedback of No Feedback. The ICU with feedback will be equipped with display device (ipod) corresponding to each Angulus device with an

interactive software interface which displays the patient's elevation and sends a color-coded cue when patients fall outside of the desired patient elevation scope. Nurses will be able to set up the display device and utilize all of its functionality including a snooze feature, which allows providers to pause the cue when patients are having a procedure, which requires they be positioned outside of the desired recumbent scope (i.e. a chest x-ray, etc.), or if the device must be removed (i.e. for bathing). Having the Angulus sensor with the corresponding display device will allow nurses to intelligibly and efficiently understand a patient's elevation and make corrections as needed throughout their workday. Nurses can decide to use this information to reposition the patients to reach the target elevation. In ICUs that are randomized to NO Feedback in Period 1, the Angulus device not have a corresponding display device and the data on patient elevation will NOT be displayed to the nurses. Nurses will continue to operate under existing clinical practices for compliance with hospital practice for elevation > 30 degrees, checking patient elevation according to existing methods. In Period 2, each ICU will cross over to the other arm and in Period 3, they will cross over back to the original arm. Three ICU (Moses MICU, Moses SICU, Weiler MSICU) will be randomized as cluster with all patients who are mechanically ventilated in those ICU randomized as a cluster to Feedback or No Feedback. During all periods of the study, *whether the bedside clinician/nurse decides to adjust the patient's body position or bed is left up to their clinical judgement.*

Statistical Analysis:

The primary outcome is compliance to head of bed elevation to 30 degree or more. This will be measured as a continuous variable between 0% and 100% compliance. This is defined as:
Compliance= 100 x ((Total time in minutes in which patients in ICU are elevated > 30 degree during period) / (Total time patients in ICU spent with Angulus device during period))
From an inferential point of view, our goal is to use the data collected by the Angulus sensor to evaluate the effect that real-time feedback mechanism has on improving compliance with patient elevation guidelines. Indeed, by automating the data collection pipeline, our study will gather patient levels with more ease and at a finer temporal scale than was previously possible.
Secondary outcomes of interest include:

1. Frequency that patients in the ICU are rotated more than 30 degree within 24 hour days and association with development of decubitus ulcers. As the technology in Angulus measures movement in 3 dimensions, it automatically records rotation in addition to elevation of patients. Another best care measure for mechanically ventilated patients is regular turning of patients to prevent formation of decubitus ulcers. This analysis will explore whether frequency of rotation for a patient is associated with subsequent development of decubitus ulcers. In this analysis, patients from all period and ICUs will be combined but the analysis will be stratified by period and ICU.
2. Frequency that patients in the ICU rotate more than 30 degree and have change in elevation of more than 15 degree within an hour and correlation with agitation as indicated by RASS. Frequent movement in patients on the ventilator can indicate agitation. RASS is a clinically collected parameter indicative of levels of consciousness and agitation.

Montefiore has 3 MICUs and all of the Montefiore ICU units has 12-16 beds. Based upon preliminary work, there are an average of 25 patients who are newly intubated each month within each ICU and the average duration of mechanical ventilation is 3 days. That translate to about 75 patient-vent days per month. Table 2 shows detectable difference given this expected sample size at different powers. We aim to conduct the study in 3 ICU over 3 months total.

Table 2. Sample Size needed based on the minimal detectable difference for mean time in range between the monitored group and the non-monitored group

| | 70% | 75 % | 80% | 85% |
|---|---|---|---|---|

| | Power | Power | Power | Power |
|---|---|---|---|---|
| Detectable Difference | | | | |
| 10% difference in means | 80 | 94 | 100 | 120 |
| 15% difference in means | 38 | 42 | 48 | 56 |
| 20% Difference in means | 20 | 24 | 26 | 30 |
| 25% Difference in means | 14 | 16 | 18 | 20 |

**Aim 4: Integrate critical end-user functionality post-implementation with an agile and iterative product development approach and assess end-user satisfaction and usability scores.**

Post implementation of the device we will utilize similar strategies deployed in Aim 1 to reassess features and functionality that end-users deem most high-value and critical, paying special attention to which new initially-identified features have diminished in importance and new features that have become known. In this phase of end-user feedback, we will also administer the Software Usability Measurement Index (SUMI) and the System Usability Scale (SUS). The SUMI is an internationally validated standard used to evaluate the quality and satisfaction of software products. The SUS is a 10-item questionnaire used for measuring perceptions of usability for multi-modal systems. It has been well documented that if staff have quality tools to work with, the overall efficiency of staff and the quality of their work output is significantly improved. Hence, it is of prime importance to us to reflect upon the reported satisfaction and usability of Angulus among end-users.

Based on the information gleaned from the successful completion of Aims 1-3, we will be well positioned to enter an iterative phase of rearchitecting Angulus. Completing the loop of the product development life cycle.

We expect to use the sensor data set captured in Aim 3 to investigate the possibility of developing software technique to prevent false alarms cause by motions due to routine nursing care. The system contains a Digital Motion Processing engine within the inertial sensor. Thus the motion sensor itself can be programmed with sensor-fusion algorithms to understand and respond to complex motion inputs. This will enable the system to recognize complex short-term patterns that correspond to routine nursing care.

By the completion of this grant, we will have tested the Angulus prototype and made significant progress toward developing Angulus 2.0. Completion of these aims will enable Angulus to conduct a larger scale efficacy trial with Phase II funding, and will position the company to pursue commercialization efforts.

**Phase I Success Criteria.** The Phase I project will have deemed to have demonstrated feasibility if the Angulus device is determined to have improved the compliance with patient elevation guidelines by 15% and there are no adverse events associated with use of the Angulus device. Ultimately, we expect a final post Phase II device to be able to improve compliance by 30% or more.

**Protection of Human Subjects**

***Protection of Human Subjects***

a. Human Subjects Involvement, Characteristics and Design

Angulus, as a product, has been developed specifically to improve compliance with patient elevation guidelines for ventilated patients in the ICU.

Aim 1 and 3 involves focus groups and surveys/questionaires of ICU care providers and hospital leaders in hospital safety and quality control who are often concerned about measuring, preventing and reporting VAP in the hospital. This will be conducted at Montefiore Medical Center and will involve anonymous participation from the respondents in which they will be queried about features and functionality of Angulus to help guide refinement of the product. No personal information or identifiers of the participants will be collected. We plan on a verbal consent from participants.

Aim 2 outlines a cluster cross over randomized clinical trial designed to evaluate the usefulness and feasibility of Angulus in a critical care setting. We will enroll ventilated patients from 3 ICUs in this trial. We anticipate that study participants will be older than 18, have an equal male to female ratio, and have poor health status. Randomization will occur at the unit-level, not the individual level, and each unit will serve as its

own control as with our current study design the assignments switch after each period. We will apply for a waiver of informed consent for data collection as this study fulfills all criteria for waiver of informed consent:

Subjects will be enrolled in the trial within 36 hours of intubation, and will remain in the trial until ICU discharge.

Participation is not limited by patients' race, sex, ethnicity or socioeconomic class, and no potential subjects will be excluded based on these criterion. We are not incorporating fetuses, neonates, pregnant women, children, prisoners or institutionalized individuals, although ventilated patients are considered to be a vulnerable population.

This is a minimal risk study. Head of bed elevation is already standard of care for ventilated patients in the ICU. However, the current practice is by "eyeballing" the patient or measuring the angle of the bed rather than the patient. Aim 3 sets out to measure the actual angle of elevation of the patient and in the active phase, provide this information to the nurses to see if it can help them improve their compliance to elevation of patient's head to prevent VAP. Angulus is a non-invasive, non-significant risk device, there are not any components, which present hazardous procedures, situations or materials to personnel and/or study subjects. Moreover, intubated patients already have a number of monitors and sensors affixed on or near them during their inpatient hospitalization. An additional sensor will cause additional complications and no other monitors or sensor will be removed in order to allow Angulus to be used.

b. Sources of Materials

In Aim 1 and 3, the sources of material will be the responses from the voluntary interviews, surveys and focus group. In Aim #2, the research material obtained from human subjects will be the data sent from the Angulus sensor and stored on the iPod touch display device. This data is stored locally and does not require the input or transmission of any PHI. The iPod touch display device is securely attached below the vital sign monitor, and each disposable sensor is assigned to a specific patient and display device. Acquired data are stored in an internal database, which cannot be accessed outside the application, and advanced features such as data export are password-protected. Data export must be performed via physical connection (i.e. via USB), onto an encrypted laptop. Additional patient level data on age, gender, BMI, and race will be collected from medical records. No identifying information will be collected.

c. Potential Risks

This is ultimately a study of compliance, and even though subjects will be assigned to active or control conditions, they will still receive the same standard of care that they are receiving now, with the potential for it to improve. Given that this is a non-significant, non-invasive mechanism, we do not anticipate there to be any psychological, financial, legal risks for subjects who are enrolled in the trial. The only risk we have identified is the potential for an allergic reaction to the adhesive. To protect against this risk, we will not enroll patients with a known allergy to our adhesive.

***Protection Against Risks***

a. Informed Consent

For Aim 1 and 3 on the focus groups and surveys on useabiity of Angulus, we will apply for a verbal consent from end-users for participation. For the purpose of Aim 2, we intend to submit a request for a waiver of informed consent, as the outcomes of this trial focus exclusively on quality improvement metrics, rather than clinical efficacy outcomes. As per 45 CFR 46.116d, Aim 3 would meet the required 4 criteria for a waiver of informed consent:

1. <u>The research involves no more than minimal risk to the subjects:</u> Angulus is a non-invasive, non-significant risk device that aims to provide real time data to nurses and other providers on compliance to elevation of the head of ventilated patients to prevent VAP. Decision about whether to change the patient's position or bed angle is still left to the bedside clinician.
2. <u>The waiver will not adversely affect the rights and welfare of the subjects:</u> Head of bed elevation does not require patient consent in current clinical care. Indeed, this is considered standard of care for all ventilated patients in the ICU.
3. <u>The research could not be practically carried out without a waiver:</u> Aim 2 proposes a cluster randomization of an ICU. It is neither practical nor possible to consent every ventilated patient in the ICU in a timely fashion as head of bed elevation is supposed to be implemented as soon as possible

after intubation and is part of the ventilator bundle orders for initiation of mechanical ventilation for patients at Montefiore.

4. When appropriate, the subject will be provided with additional pertinent information after participation. We do not anticipate any information from this trial will be pertinent to the patient's health or clinical outcome as elevation of head is already standard of care for patients in the ICU.

b. Protections Against Risks

To minimize the possibility of a data breach, all data will be de-identified and stored in encrypted databases to prevent the possibility for any potential breach of PHI. No names or HIPAA identifiers will be associated with computerized data files and similarly any published materials will represent de-identified aggregate data. Data collected from the sensors will be stored locally on the display device prior to being downloaded. Data will be downloaded to a secure encrypted laptop upon patient discharge.

In order to ensure strict adherence to HIPAA compliance, no data will be sent over wireless networks, and all downloaded data will be stripped of any potential patient identifiers.

In order to adhere to infection control and patient safety standards, over the course of both phases of the study, the Angulus hardware component will be enclosed in a disposable encasing with disposable adhesive. Additionally, the display devices will be encompassed in a disposable protective case to prevent the carry over of any infectious organisms during patient turnover. The only re-usable component of this mechanism is the sensor itself (which is then enclosed in a disposable encasing).

To minimize the potential for any physical adverse reactions, we will exclude any patients with a known allergy to our adhesive.

***Potential Benefits***

Under our current study design and hypothesis, we are proposing that implementation of the Angulus sensor with corresponding data display will improve compliance with patient HOB guidelines. This could be a potential benefit of the research to participants. Since adherence to patient elevation guidelines are currently low, and patient elevation has been shown to have a significant impact on the development of VAP, increasing compliance in this domain could greatly improve the quality of care ventilated patients are receiving.

***Data and Safety Monitoring Plan***

While we do not intend to establish a formal Data Safety Monitoring Board (DSMB), we will abide by local and regulatory requirements for reporting adverse events (AEs) to local and federal regulatory agencies in a timely manner. Any adverse events identified by the study team or providers will be reported to the study coordinator and both PIs, and appropriately recorded and sent to the necessary regulatory entity for review.