

New Concept in Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)

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Abstract: The world-wide impact of traumatic injury and associated hemorrhage on human health and well-being is significant. Methods to manage bleeding from sites within the torso, referred to as non-compressible torso hemorrhage (NCTH), remain largely limited to the use of conventional operative techniques. The overall mortality rate of patients with NCTH is approximately 50%. Studies from the wars in Afghanistan and Iraq have suggested that up to 80% of potentially survivable patients die as a result of uncontrolled exsanguinating hemorrhage. The commercially available resuscitative endovascular balloon occlusion of the aorta (REBOA) is a percutaneous device for the rapid control of torso hemorrhage in trauma. A compliant balloon is inserted via the femoral artery and inflated in the thoracic or abdominal aorta, providing inflow control of the abdomen, pelvis, or groin/lower extremities. Recent studies indicate that REBOA carries an inherent risk of aortic injury due to over-inflation and possible risk of aortic or iliac artery rupture. A new approach is to resolve the issue of balloon sizing and over-inflation. We propose a novel concept to be used in trauma facility for arterial occlusion to eliminate arterial injury and the risk of vascular rupture through real time balloon diameter profile measurements to ensure proper inflation. The proposed concept, called Smart Resuscitative Endovascular Balloon Occlusion (SREBO) will be novel in the following aspects: 1) It will have electrical conductance-based navigation technology to target the desired site of balloon deployment in the aorta, 2) The balloon can determine the time of proper inflation using electrical conductance catheter technology. This technology would eliminate the risk of arterial rupture and simplify the procedure in the trauma facility or medical clinics without significant training. The results can be displayed on a handheld device. This novel device has the potential to save civilians in trauma or soldiers injured on the battlefield.

Keywords: REBOA; hemorrhage; balloon catheter; conductance catheter

1 Introduction

Vascular injury with concomitant hemorrhage is the leading cause of potentially preventable death in both civilian and military trauma patients. Of the 1.8 million patients in the 2007-2009 National Trauma Data Bank, 249,505 met the anatomic criteria for potential non-compressible torso injury (NCTI). Of these, 8% patients had associated major hemorrhage, or NCTH. The rate of pulmonary and torso vessel injury was similar (53.4% and 50.6%, respectively). The overall mortality rate of patients with NCTI and NCTH was 6.8% and 44.6%, respectively [1]. Studies from the wars in Afghanistan and Iraq have suggested that up to 80% of potentially survivable patients die as a result of exsanguination [1]. These studies categorize



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bleeding broadly as compressible or non-compressible, depending on whether the hemorrhage control measures can be applied externally and immediately at the point of injury, or whether they require operative exposure for hemorrhage control.

Compressible hemorrhage originates from extremity or junctional (groin, axilla, neck) injuries and can be managed by direct application of pressure/dressings or a tourniquet. The reemphasis on tourniquet use has increased survival from compressible extremity hemorrhage to greater than 90% [2]. In contrast, methods to manage bleeding from sites within the torso, referred to as non-compressible torso hemorrhage (NCTH), remain largely limited to the use of conventional operative techniques and thus cannot be performed outside of a fully staffed operating room [3].

Four categories of torso injury, each based on vascular disruption, were identified: (1) Thoracic, including lung; (2) Solid organ (high-grade spleen, liver, and kidney); (3) Specific axial vessel; and (4) Pelvic fracture with ring disruption. Of 15,209 injuries sustained during the study period, 12.7% had sustained one or more categories of torso injury. The highest mortality injury complexes were identified as major arterial injury and pulmonary injury [3]. In this paper, we briefly cover the present practice and introduce a new concept to eliminate the inherent risks associated with REBOA.

2 Present Practice

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a percutaneous technique for early temporary control of torso hemorrhage in trauma. A compliant balloon is inserted via the femoral artery and inflated in the thoracic or infrarenal aorta, providing inflow control of the abdomen or pelvis, respectively [4]. The balloon is inserted in the artery, and inflated with a saline solution while the arterial blood pressure is continuously measured by arterial pressure monitoring system. The inflation stops when the arterial pressure elevates which is an indication that the balloon covers the whole lumen opening and thus occludes the vessel. To expedite deployment, inflation is frequently performed as a blind technique with minimal imaging, which carries a risk of vessel wall injury. Originally, this technique was described using conventional endovascular equipment, consisting of large sheaths, wires and balloon catheters, guided by fluoroscopy. In an effort to expedite the procedure, smaller caliber balloon catheters have been developed, which do not require a wire or fluoroscopic imaging [4]. Of particular concern are patients with small caliber aortas that receive balloon inflation without radio-graphic guidance, or patients where the balloon is mistakenly inflated while still in the smaller diameter iliac arteries. The issue of balloon overinflation has been investigated using explanted porcine aortas that characterized the relationship between balloon inflation and aortic deformation, including aortic rupture risk [5]. The study results indicate that inflation of aortic balloon catheters carries an inherent risk of aortic injury. The study concludes that smaller diameter aortic segments undergoing over inflation are at higher risk of aortic rupture.

The desired anatomic target for REBOA deployment is either in Zone 1 (balloon catheter may be inflated at the distal thoracic aorta for control of severe intra-abdominal or retroperitoneal hemorrhage), or in Zone 3 (balloon catheter may be inflated at the distal abdominal aorta for patients with severe pelvic, junctional, or proximal lower extremity hemorrhage) [6]. Due to the known NCTH epidemiology as well as the common inability to exactly locate the source of hemorrhage prior to surgical exploration, the majority of REBOA utilization and deployments are in Zone 1 (descending thoracic aorta).

Chen et al. [7] examined the microscopic behavior of collagen and elastin fibers in porcine coronary arteries. They demonstrated that collagen and elastin fibers become maximally aligned at a circumferential stretch ratio of 1.8, suggesting that this stretch ratio is the upper limit of vessel distention. Teng et al. [8] examined human atherosclerotic carotid arteries and demonstrated a stretch ratio failure point of around 1.7. These results demonstrate that REBOA inflation has potential of vessel injury at high levels of inflation or stretch. Balloon positioning in the right zone is another shortcoming of the existing REBOA. Furthermore, blind navigation of the REBOA without the use of x-ray can be time consuming and uncertain.

A recent publication points out the need for safe and adequate balloon inflation, and suggests an objective indicator reflecting occlusion of the aorta is necessary [9]. There is currently no single established

objective indicator. Despite careful conduct of the workflow, aortic rupture caused by over-inflation of the balloon can occur because of the absence of such an indicator.

3 New Concept Device

In response to the need for accurate balloon sizing, a novel sizing conductance catheter/balloon (SCB) system that provides accurate, real-time balloon size assessment during inflation/deflation has been developed [10-12], thus providing a method to measure vascular annulus accurately and objectively within the current workflow procedure for coronary, peripheral or valvular applications [10-12]. SCB sizing is accomplished using simple, physics-based electrical conductance measurements on a standard balloon catheter. This has been shown in other applications [13,14-16] that electrical conductance measurements are a safe and highly effective method for assessing luminal organ size based on a fundamental law of physics (i.e., Ohm's Law-see Theory below). The annulus size can be determined accurately by stimulating a small, safe, and alternating electrical current within the balloon during inflation and apposition against the wall. The electrical conductance-based sizing measurements are made in real-time during balloon inflation, displayed on an easy-to-read console screen, and provided as an objective sizing assessment (no manual measurements or interpretation are required by the physician). The SCB catheter is easy (i.e., functions as a standard balloon) and only requires a simple, sterile hook-up to a bed-side display console (i.e., future work can make this hook-up wireless). Since there is no physician required calibration of the SCB, the use of the device fits easily within the current workflow procedure (i.e., virtually no added time). The balloon provides accurate sizing results with various types of saline mixtures used during inflation/deflation and can accurately size the full range of possible annular sizes (e.g., ~20-30 mm) since the conductance measurements are made inside the insulative balloon, which allows for excellent accuracy in any environment. Thus, the SCB catheter provides an innovative, clinically-relevant, real-time, simple, accurate, repeatable, and objective sizing measurement during balloon inflation which eliminates the possibility of over-inflation which could result in arterial rupture.

It is feasible to navigate to the injury site for the occlusion of the arterial injuries without balloon overinflation and potential vessel injury by combining this technology with the navigation technology. This combined system may be referred to as "Smart Resuscitative Endovascular Balloon Occlusion (SREBO)". Proper inflated balloon has round distal and proximal end shape while square edges represents potential over-inflation. The smart catheter takes advantage of this phenomena for proper balloon inflation by measuring the diameter profile at several positions along the length of the balloon. The balloon pressure is also measured in real time by installing a pressure sensor inside of the balloon to confirm that the balloon has apposed the wall as denoted by initial increase in pressure. Another advantage of the proposed technology is the ability to locate the site of injury which is absolutely necessary to expedite the procedure occlusion procedure. The combination of diameter profile, navigation system and pressure measurements will be an ideal indicator as to when the balloon covers the lumen of vessel without over-inflation. Rapid and safe control of major hemorrhage will save lives and reduce morbidity in civilian trauma and on the battle field. In principle, the systems can be used in trauma centers or medical clinics and is relatively simple (i.e., does not require significant training) as demonstrated by prior applications [9-11].

3.1 Theory of Conductance Based Sizing

The SCB catheter system [17] is founded on a physical law of electricity (Ohm's Law) which provides a physical basis for how the balloon diameter is measured during inflation. The SCB catheter contains two electrodes on the outer edge of the balloon that inject a constant current (I) between them inside the balloon. There are five sets of electrode pairs (measurement sites) in-between these outer electrodes and each pair measures a variable voltage drop (V) inside the balloon. The ratio of the constant current and variable voltage between any of the electrode pairs (i) is the total conductance for each electrode pair set ($G_i = I/V$). When inflated, Ohm's Law (Eq. (1)) states that the total measured conductance at any electrode pair (i) inside the balloon (G_i) is related to the local inner cross-sectional area (CSA_i) of the balloon, the electrical conductivity (σ) of the saline used to inflate the balloon, and the spacing between the measurement electrodes, (center to center, L) is given by:

$$G_i = I/V = CSA_i * \sigma/L$$

(1)

The G_i value is measured across each i_{th} electrode pair and displayed by the console, σ is constant for the fluid injected inside the balloon (a mixture of saline with a predetermined and known value), and L is a known constant (the fixed spacing between inner electrodes; L = 2 mm). CSA_i, and hence the inner balloon diameter, can be calculated by solving Eq. (1) and adding twice the wall thickness (wt) of the balloon as such: Diameter_o = $\sqrt{(4*G_i*L/(\pi*\sigma)) + 2*wt}$ (2)

Since all other variables are known, Eq. (2) shows that the balloon size is directly proportional to G_i . Given the continuous G_i measurement on the console, Eq. (2) can be instantaneously solved for the diameter which can be displayed on the console to provide real-time clinical feedback about vessel size (see Fig. 1-right bottom for an example). Although G_i is the main variable that relates directly to CSA, the value of σ can sometimes vary and impact system accuracy. The σ term expresses the inherent ability of the fluid inside the balloon to conduct electricity and varies based on two key variables: 1) Temperature of the fluid inside the balloon and 2) Type of fluid inside the balloon. The σ dependence on temperature is linear and already characterized by for other applications [12-16]. Thus, by measuring the temperature inside the balloon during inflation using a thermistor, any variations in temperature that arise to maintain excellent sizing accuracy can be adjusted [14]. The SCB catheter system was designed and built for the development of a novel sizing valvuloplasty conductance balloon catheter system that functions as a typical valvuloplasty balloon catheter, but with additional functionality for accurate display of real-time balloon size for aortic annulus assessment [11]. This system is described below.



Figure 1: Left) SCB catheter. Top Right) Balloon close-up showing the multi-electrode design with thermistor. Bottom Right) Easy-to-read bedside console display for real time SCB measurement (right) next to a monitor for balloon inflation pressure (currently used in the catheterization lab)

3.1.1 Device Characteristics

The SCB catheter system consists of three components: 1) SCB catheter, 2) Connector cable, and 3) Console (Fig. 1). The SCB catheter functions as a standard balloon with a 6Fr diameter, 140 cm length body, a 20-30 mm diameter 50 mm long compliant balloon, an inner lumen, and a standard proximal port for balloon inflation (Fig. 1-left). The balloon diameters range from 20-30 mm depending on the application with a standard set of radiopaque outer electrodes that mark the edges of the balloon. The outer marker electrodes also serve an additional purpose for the SCB by stimulating a constant electrical current between them. The electric current stimulated within the balloon is an alternating 136 μ App, 10 kHz waveform, which has already been shown to be safe when stimulated directly within the vasculature [10-15] and thus is even more safe given the insulative nature of the balloon. During balloon inflation and deflation, additional sets of five electrodes in between these outer electrodes spaced ~1mm apart make voltage/balloon

sizing measurements (Fig. 1-top right; in the center of the balloon there is a row of six electrodes, which make up five pairs of electrodes when grouping them in successive pairs of electrodes). The multiple measurements made inside the balloon profile can be used to locate the minimum diameter during inflation which corresponds to the aortic valve annulus (i.e., valvuloplasty balloons are semi-compliant and often take on a "dumbbell" shape during inflation with the minimum valve corresponding to the aortic valve annulus by anatomical definition). Thus, instead of having just one set of electrodes in the middle of the balloon and requiring the physician to place and maintain these electrodes in the center during inflation, the device has multiple electrode pairs along the length of the balloon. The SCB catheter requires no physician calibration and can be disconnected/reconnected to console at any time. A sterile connector cable (not shown) easily attaches to the proximal electrode connector of the SCB and the display console.

The console is a monitor and data acquisition system that: 1) generates the safe current across the outer balloon electrodes, 2) measures voltage drops across the inner balloon electrodes, 3) calculates the balloon diameter based on Ohm's Law, 4) balloon pressure, and 5) displays the profile data in real-time on the screen.

SCB bench and in vivo sizing shows accurate and repeatable sizing results across a full range of possible aortic valve annulus sizes. SCB measurements were made in uniform and non-uniform 18-30 mm diameter phantoms on the bench, while *in vivo* measurements were made in the aortic valve in three (3) healthy swine of different weights (35-60 kg) and thus different sized aortic valve annuli (i.e., ~20-30 mm diameter) during high-rate pacing at 170-220 bpm (clinical practice during valvuloplasty). Accuracy was determined by comparing SCB measurements to the known dimension (bench) or the quantitative angiographic assessment (in vivo). System repeatability was determined by comparing consecutive repeat SCB measurements to each other. Both bench and *in vivo* results were excellent with an average accuracy root mean square (RMS) error of 2.4% and repeatability accuracy of 0.6%. There was a small and clinically insignificant difference for the accuracy and repeatability measurements (accuracy difference = 0.3 ± 0.5 mm; repeat difference -0.03 ± 0.1 mm), which shows no bias in the SCB catheter system. Linear regression showed a nearly perfect linear relationship between the SCB measurements and the true/known dimension (Accuracy: SCB = 1.01*Known; R² = 0.98) and repeat SCB measurements (Repeatability: SCB#1 = 1.0*SCB#2; $R^2 = 1$) where "Known" means size of the phantom that we know, #1 and #2 are duplicate measurements. The insulative environment of the balloon allows for these highly accurate and repeatable results to occur on the bench and in vivo.

3.2 Navigation System

A novel navigation and tip location technique has been developed that can be utilized for the current application. The conductance guidewire (CGW) system uses electrical conductance recordings to assess changes in vessel cross-sectional area to guide navigation of the guidewire or catheter tip. Electrical conductance rises with increase in diameter and drops with decrease as per Ohm's law. Bench and *in vivo* studies in six swine were used to confirm the accuracy and repeatability of the placement at various anatomical locations. The guidewire tip location was confirmed by direct visualization *vs.* the desired location. Results indicates that CGW PICC (Peripherally Inserted Central Catheter) guidance is highly accurate and repeatable with virtually no difference between actual and desired tip location. The difference between the CGW catheter location *vs.* the desired target was 0.7 mm (6.6% error) on the bench and 0.4 mm (5% error) *in vivo*. No complications or adverse events occurred during CGW usage [9,18].

The CGW system provides navigation and tip location feedback to the clinician through a console screen display that shows changes in conductance and oscillations during CGW advancement. The complete CGW system consists of three components as shown in Fig. 2: CGW, connector handle, and console. The CGW is a 180 cm guidewire consisting of a floppy/atraumatic distal tip, a tetrapolar measurement electrode section, a long-coiled body around a solid core, and a stiff proximal end for easy manipulation and attachment to the connector handle. The excellent mechanical properties of the CGW allow for easy steerability, withdrawal, and re-advancement when conductance feedback demonstrates that navigation is occurring in the wrong direction away from the target junction. The connector handle allows

for connection of the CGW for measurements and disconnection of the CGW for over-the-wire device delivery with no need for calibration. The console continually displays the conductance results and provides feedback about the catheter position. The console provides this feedback by injecting a small, safe amount of alternating electric current (AC) through the distal outer electrodes of the CGW and acquiring, filtering, and displaying the measured conductance across the distal middle electrodes.



Figure 2: CGW guidewire (top left), connector handle (top middle), and console (top right)

This device has previously been tested [18] to advance the catheter towards the superior vena cava (SVC) and to the right atrium (RA). During advancement of the CGW from the initial access vein (typically the cephalic, brachial, basilica, or saphenous vein) to the axillary vein, the subclavian vein, the brachiocephalic vein, the SVC, and the RA, the measured conductance show step increases as the guidewire reaches a new, larger vessel, while navigation away from the SVC/RA results in decreases in conductance. The point at which there is the largest absolute conductance coupled with large pulsatile conductance changes denotes the location of the cavoatrial junction. When the CGW has located the region of interest for catheter placement, the CGW is held in place, and the catheter is advanced over the wire until the measured conductance drops very abruptly to nearly zero.

The tip navigation and location technology can be used to navigate the REBOA catheter by placement of the tetrapolar electrodes at the distal tip of the device. The integration of the tip navigation and location with the sizing profile balloon can address some of the outstanding shortcomings of the REBOA technology.

4 Discussion

NCTH remains the recognized "holy grail" in terms of methods to achieve early hemorrhage control in modern battlefield and civilian trauma care. REBOA is one of the only available and an increasingly accepted technique used as a less invasive alternative for controlling bleeding in patients with NCTH. Despite the obvious benefits, the potential for major vascular complications and device failures must be addressed and resolved for the procedure to be used in widespread applications. Some of the major specific complications are balloon positioning and over-inflation during occlusion without arterial injuries and balloon rupture. A novel concept has been proposed to deal with the both complications which requires implementation and validation in future studies. The goal is to accomplish the following requirements: 1) diameter profile measurement capability, and 2) aorta navigation and balloon location capability. These capabilities should be assembled in a single device referred to as "Smart Resuscitative Endovascular Balloon Occlusion (SREBO)" to address some of the current shortcomings and the risk profile of REBOA in the setting of NCTH.

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