



Pilot Study to Evaluate a Novel Non-Invasive Technology to Measure Peripheral Venous Pressure

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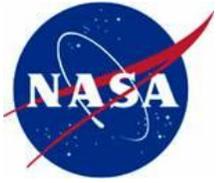
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Table of Contents

Table of Contents.....	i
ACRONYMS.....	ii
ABSTRACT	iii
INTRODUCTION.....	1
METHODS	1
<i>Non-Invasive Peripheral Venous Pressure</i>	2
<i>Invasive Peripheral Venous Pressure</i>	4
<i>Statistical Methods</i>	4
RESULTS	5
<i>Cephalic Vein</i>	5
<i>Greater Saphenous Vein</i>	6
<i>Jugular Vein</i>	6
<i>Supratrochlear Vein</i>	7
DISCUSSION.....	8
<i>Limitations of the Study</i>	10
CONCLUSIONS	11
ACKNOWLEDGMENTS	11
REFERENCES	11

ACRONYMS

CVP	central venous pressure
C	Celsius
F	Fahrenheit
ICP	intracranial pressure
IPVP	invasive peripheral venous pressure
MHz	megahertz
mmHg	millimeters of mercury
NASA	National Aeronautics and Space Administration
NIPVP	non-invasive peripheral venous pressure
PVP	peripheral venous pressure
VIIP	Visual Impairment/Intracranial Pressure syndrome

ABSTRACT

Understanding the vision changes observed in astronauts who participate in long-duration spaceflight has become a high priority at NASA. The Visual Impairment/Intracranial Pressure (VIIP) syndrome has been hypothesized to be related to cephalic fluid shifts and possibly venous congestion secondary to elevations of central venous pressure (CVP). The resulting venous congestion may inhibit drainage of cerebrospinal and lymphatic fluids from the skull and consequently increase intracranial pressure (ICP). Due to the invasive nature of direct CVP measurement, it has not been collected beyond the first few days of spaceflight. An alternative to invasive measurement of CVP is to estimate CVP by non-invasively measuring peripheral venous pressure (PVP) using a novel method called compression sonography. In this technique, a vein is visualized using ultrasound, and then the downward pressure of the probe is gently increased until the vein collapses. The pressure required to collapse the vein is measured using a pressure transducer (VeinPress 2010, Vein Press GmbH, Switzerland) attached to a commercially available ultrasound probe and is directly related to venous pressure. Using the Vein Press, we sought to determine the feasibility of using compression sonography to obtain non-invasive measures of PVP in four veins: the supratrochlear vein in the forehead, the jugular vein in the neck, the cephalic vein in the arm, and the greater saphenous vein in the leg. Baseline measurements were obtained prior to inducing a physiologic perturbation to increase pressure within the vein, at which point measurements were recorded to determine the ability to non-invasively detect pressure changes. Furthermore, we compared these non-invasive measures of PVP in two veins to invasive measures obtained from a venous catheter with an in-line pressure transducer. Intra- and inter-operator variability of non-invasively acquired PVP also was assessed in all veins. The sonographers were able to measure PVP in each vein with each condition, and as expected, observed appropriate responses to various conditions that yielded an increase in venous pressure. In the greater saphenous and cephalic veins for which invasive measurement was available for comparison, non-invasive PVP was consistently underestimated compared to invasive PVP but became more accurate as the study progressed, suggesting a learning curve that contributes to the reliability of non-invasive PVP measurements. Image degradation due to the Vein Press may be a potential limitation, especially in smaller veins where measurements are more difficult to obtain. Our experience suggests that vessel size and sonographer experience can contribute to variability of results. Despite deviations of the non-invasive measures from those of invasive PVP, we have shown compression sonography has potential for the determination of venous pressure trends in selected veins and is more reliably obtained in larger vessels.

INTRODUCTION

Greater than 40% of American astronauts have developed permanent changes in visual acuity after long-duration spaceflight (10). Astronauts taking part in short-duration missions have experienced reversible changes in vision without permanent alterations to the eye. However, observations of post-flight data have indicated the permanence of ocular perturbations as a potential consequence of microgravity exposure as defined by the VIIP syndrome. These changes include papilledema, choroidal folds, posterior globe flattening, and dilation of the optic nerve sheath with varying degrees of severity (5, 9, 14). Susceptibility to this syndrome could be influenced by genetics, anatomical variation, or other unknown factors. It is currently hypothesized that these changes in vision may be related to elevated central venous pressure (CVP). An elevated CVP may inhibit drainage of cerebral spinal and lymphatic fluids from the skull and thus contribute to increased intracranial pressure (ICP), as has been observed in an experimental canine model (8). Understanding the contribution of the loss of gravity-assisted drainage of venous blood from the brain is critical to the understanding of the VIIP syndrome and minimizing the risks of increased ICP in astronauts who embark on exploration missions beyond low-Earth orbit.

Data from a limited number of space shuttle astronauts suggest that CVP either decreases or does not change upon entry into microgravity (6, 11). These direct, invasive measures of CVP have been obtained in a small number of astronauts who were instrumented with an intravascular pressure transducer before and for up to two days of microgravity (3, 4). Unfortunately, no data currently exists beyond this point, and the current data available from post-flight measurements are inconclusive. In light of the limited data available, it is important to find a non-invasive method of CVP measurement to provide further insight into the nature of the VIIP syndrome.

Direct measurements of CVP may present potential medical complications due to the invasive nature of catheter insertion into a subclavian, internal jugular, or peripheral vein (1, 12), and would be difficult to assess in the large number of subjects required to fully understand CVP throughout the duration of a long-duration mission. Therefore, an alternative is to estimate CVP from a non-invasive measure of peripheral venous pressure (PVP). A novel technique to estimate PVP, called compression sonography, has been developed using a pressure transducer in conjunction with ultrasound imaging of the vein in question. There has been a strong correlation between PVP determined by this non-invasive measurement and invasive measurements in both healthy subjects and critically ill patients (2, 13), but the feasibility of non-invasive PVP measures as a research tool has not yet been tested.

We sought to determine the validity of compression sonography in selected veins by comparing the non-invasive measures of PVP in two veins to invasive measures obtained from a venous catheter with an in-line pressure transducer. Repeatability of non-invasive venous pressure measurements were evaluated in four different veins during rest and under conditions of elevated venous pressure. Finally, we assessed intra- and inter-operator variability of non-invasively acquired peripheral venous pressures.

METHODS

This pilot study was approved by the NASA Johnson Space Center Institutional Review Board, and written informed consent was obtained from each test subject. Ten volunteers (five male, five female)

participated in testing on four separate days. Subjects were asked to abstain from nicotine for twelve hours and high-fat foods for four hours prior to each session. Room temperature was maintained between 21.1-23.8° (70-75°F), and heating pads were placed on the arm, lower leg, and core, to maintain the body temperature of the subject as needed in order to prevent temperature-induced venous constriction.

We assessed the validity of non-invasive PVP measures in four veins: cephalic vein (forearm), greater saphenous vein (lower leg), internal jugular vein (neck), and supratrochlear vein (forehead). For the purposes of our investigation, it is necessary to apply just enough pressure to compress the selected vein. Therefore, only superficial veins overlying a relatively firm structure (i.e., bone, trachea) may be evaluated with this method. These requirements, along with relevance to microgravity research, drove our selection of vein sites.

A 20-minute supine rest period preceded testing. During this time, catheters were inserted in the cephalic and greater saphenous veins while sonographers conducted preparatory scans of the vessels to be imaged, marked their locations, and applied blood pressure cuffs to the arm and leg. Distance from the scanning site to an anatomical landmark was measured in order to ensure data were consistently obtained from the same location on subsequent days.

We sought to correct for the height difference between the imaging sites and heart level in our statistical models. Vertical distance between the imaging sites, the right atrium of the heart and the floor were obtained each testing day. Since head-down tilt was necessary to elevate PVP for the evaluation of the jugular and supratrochlear veins, vertical distance to the imaging sites from the floor were measured at baseline and with tilt angle change. During the first session, the vertical distance between the chest wall and a right atrial location on the atrial side of the tricuspid annulus was assessed by 2-dimensional ultrasound. The combination of these numbers provided an estimation of the hydrostatic gradient between the imaging sites and the right atrium.

Non-Invasive Peripheral Venous Pressure

Non-invasive PVP (NIPVP) measures were obtained by the two sonographers in a randomized but balanced order for each vein in each of three conditions. Each sonographer obtained a total of five NIPVP measurements for each vein under each condition. For the greater saphenous and cephalic veins, PVP (non-invasive and invasive) was measured at baseline supine followed by partial occlusion of venous flow with a blood pressure cuff (Hokanson E20 Cuff Inflator, Hoaknson, Bellevue WA) located proximal to the measurement site and inflated to 30 and 60 mmHg. Cuff pressures were validated with the use of a pressure sensor (Validyne PS309, Validyne Engineering Corp., Northridge, CA) at each cuff inflation pressure. While performing measurements on the cephalic vein, the forearm was placed on a table below heart level with the elbow at approximately 60° to allow for increased venous filling in the vein and therefore improve ultrasound imaging. For the jugular and supratrochlear veins, PVP (non-invasive only) was measured while supine and at 10° and 20° head-down tilt. Given the influence of respiration on intra-thoracic and consequently internal jugular pressure, all jugular vein measurements were obtained at end expiration. Due to the peripheral location of the other vein sites, there was no discernable pressure difference with respiration.

We used a custom-made device (Vein Press 2010, Vein Press GmbH, Switzerland) consisting of a commercially available pressure transducer attached via flexible tubing to a bladder filled with an

ultrasound-translucent mixture of water and glycerin. The bladder was attached to the head of a 12-5 MHz linear array probe on commercially available ultrasound equipment (GE Vivid Q, GE Healthcare, Milwaukee, WI, see **Figure 1** below). Preliminary training was provided to the sonographers by the manufacturer of this device.

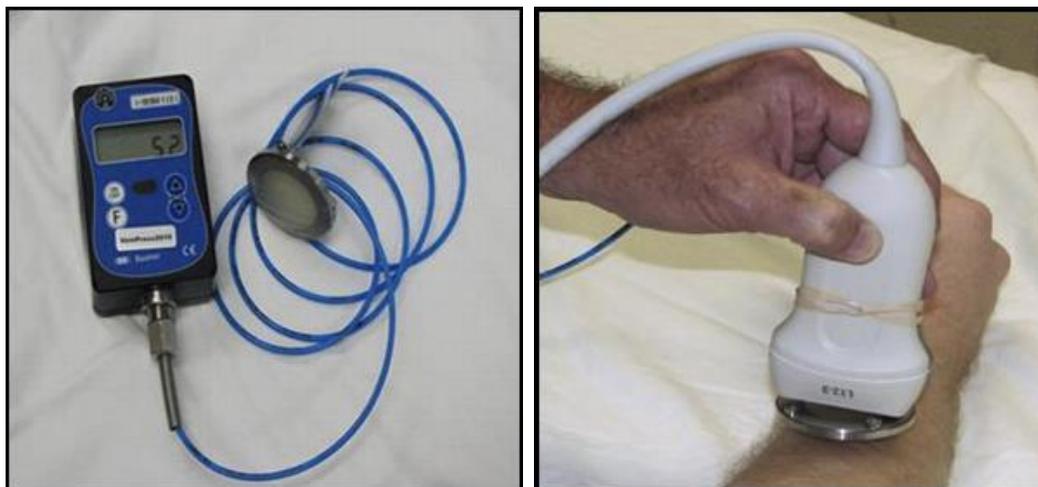


Figure 1. VeinPress device by itself (left) and positioned as it was used on the head of the ultrasound probe during cephalic vein pressure measurements (right).

Measurements for all veins were obtained using a standardized protocol. Beginning with baseline, the sonographer placed the bladder against the skin overlying the vein of interest without compressing and, after zero adjustment of the Vein Press, slowly applied pressure until the vein was compressed to the point of closure, which was verified by ultrasound imaging (**Figure 2**). According to Laplace's law, the pressure applied by the bladder on the skin that was necessary to compress the vein was assumed to equal the pressure within the vein. The pressure in the bladder was displayed digitally to an independent operator so that each sonographer would be blinded to their own results and those obtained by the other sonographer. Once the operator recorded the measurement upon visualization of venous closure, the sonographer returned the transducer to its original position for at least 10 seconds before repeating the measurements four more times. Upon completion of the first sonographer's measurement set, the second sonographer repeated the same procedure. Thereafter, a physiologic perturbation was initiated to increase venous pressure in the same vein and the process was repeated for both sonographers until all vessels and conditions were evaluated. Following each change in tilt angle or cuff inflation, there was a stabilization period of two minutes during which no measurements were taken.

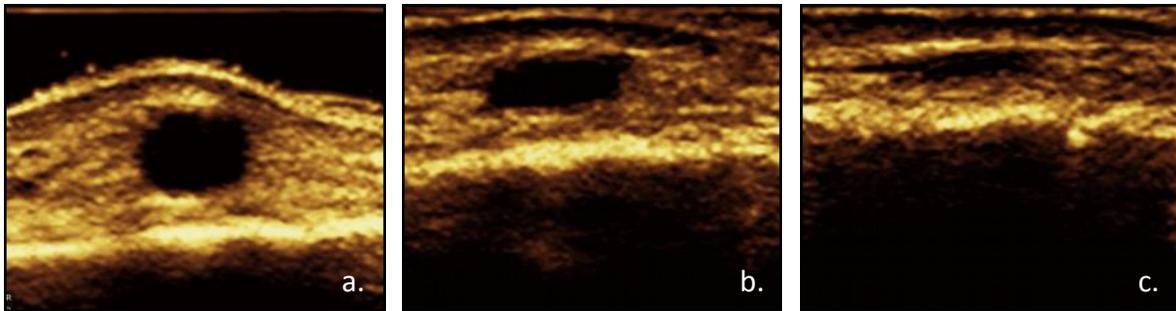


Figure 2. An image of an uncompressed vein is shown on the left (a). The middle image (b) shows a partially compressed vein. The image on the right (c) displays a fully compressed vein.

For all scans, sonographers ensured the vessel in question was in the middle of probe standoff, since this position was found to be most sensitive to changes in the pressure applied with the bladder and assisted with standardization of scanning technique. It was also necessary to ensure that the tubing of the Vein Press device was not compressed or moved during data acquisition, as agitations of the fluid in the tubing influenced results.

Invasive Peripheral Venous Pressure

Invasive PVP (IPVP) measures were only measured in the cephalic and greater saphenous veins using a Draeger Infinity Delta XL (Draeger Medical Systems, Inc., Danvers, MA) for comparison to non-invasive measurements. During the 20-minute rest period, a registered nurse inserted an intravenous catheter attached to an in-line pressure transducer into the greater saphenous and cephalic veins to a point just distal to the NIPVP measurement site. Using a laser level, the pressure transducer was zeroed to the same level as the catheter. IPVP measures were taken immediately before and after non-invasive measures during baseline rest and with the blood pressure cuff inflated to 30 and 60 mmHg.

Statistical Methods

For the cephalic and greater saphenous veins, IPVP and NIPVP blood pressure measurements were first averaged over replicate measurements (normally 5 for NIPVP, 2 for IPVP) within each combination of subject, operator, session, and cuff pressure. For each of these veins, we used linear mixed-effects regression models (7) to characterize the relationship between the two types of measurements and for making statistical inference about *a*) the accuracy of the non-invasive method, assuming the invasive method to have negligible error, *b*) possible reliability growth in the non-invasive measurements throughout the duration of the study, *c*) the effect of operator, and *d*) the effect of vertical distance between the point of measurement and the heart. However, even after averaging over replicates, mixed-model estimates of regression lines were too dependent on a few outlier measurements to allow proper statistical inference or accurate model-based estimation. Therefore, we re-estimated model parameters with some outliers removed (defined as values with significant deviation from the center line of the residuals) to obtain an approximate evaluation of the bias, gain and variability of the non-invasive measurements under the assumption that the range and variability of the data with outliers removed would be typical of what could be expected under ideal conditions with aptly trained operators.

For the jugular vein, IPVP measurements were not made, so neither the accuracy of the invasive method or a reliability growth model could be estimated. However, we also used a mixed model to

estimate the responsiveness of the NIPVP to tilt angle and to make inference on the effect of operator and vertical distance. For the supratrochlear vein, the same sort of inferential tests were made as for the jugular vein, however, it was first necessary to do further averaging over sessions for each subject-operator-tilt combination to make statistical model assumptions more realistic.

RESULTS

Cephalic Vein

A scatterplot of the NIPVP vs. IPVP measurements is displayed in **Figure 3** below for all subjects, sessions, and both operators. In this figure, each point represents an average of up to 5 NIPVP replicates (outliers removed) and 2 IPVP replicates. Trend lines for Operator 1 estimated from the mixed-effects linear regression analysis are superimposed. On average, the non-invasive measurements were higher for Operator 2, than for Operator 1 ($p = .004$); however, the estimated mean difference was only 1.8 mmHg. Therefore, similar trend lines for Operator 2 are omitted in this figure. It is clear that although there is a general trend for NIPVP to increase with IPVP, there is considerable variability in the non-invasive measure, and this variability increases as IPVP increases. On average, the slope describing the gain of the non-invasive measure for every unit of increase in the invasive measure was far less than the ideal gain of 1.0 (dashed line) ($p < .0001$), a necessary condition for unbiased estimation. However, the gain was found to increase significantly ($p < 0.001$) as the study progressed over 14 weeks, perhaps reflecting operator learning or improved, non-invasive measurement techniques. The three lower lines in Figure 3 represent separate estimates of the gain with slopes of 0.21, 0.35, and 0.48 for 0, 7, and 14 weeks, respectively. Thus, for this vein, even for operators with 14 weeks of experience, we would expect the NIPVP measure to be only about 50% responsive (on average) to the actual change in pressure.

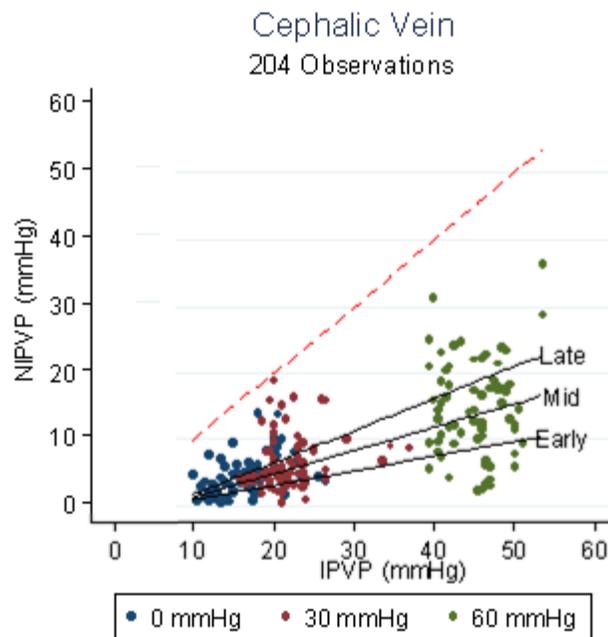


Figure 3. NIPVP vs. IPVP for the cephalic vein. The lines labeled “Early,” “Mid,” and “Late” display a trend for the NIPVP to more closely approximate IPVP with increased sonographer experience. The dashed red line is the line of identity.

Greater Saphenous Vein

A scatterplot of the NIPVP vs. IPVP measurements is displayed in **Figure 4** below for all subjects, sessions, and both operators. As in Figure 3, each point represents an average of up to 5 NIPVP replicates and up to 2 IPVP replicates. For this vein there was no evidence of a differential operator effect ($p = 0.86$). As with the cephalic vein, there was a tendency for the NIPVP to increase with IPVP, but with considerable variability, and this variability increased as IPVP increased. The estimated slope describing the gain of the non-invasive measure for every unit increase in the invasive measure was 0.56, again far less than ideal gain of 1.0 (dashed line) ($p < .0001$). Since there was no discernible effect of study week on this slope ($p = 0.525$) or the intercept ($p = .143$), only one trend line is shown here.

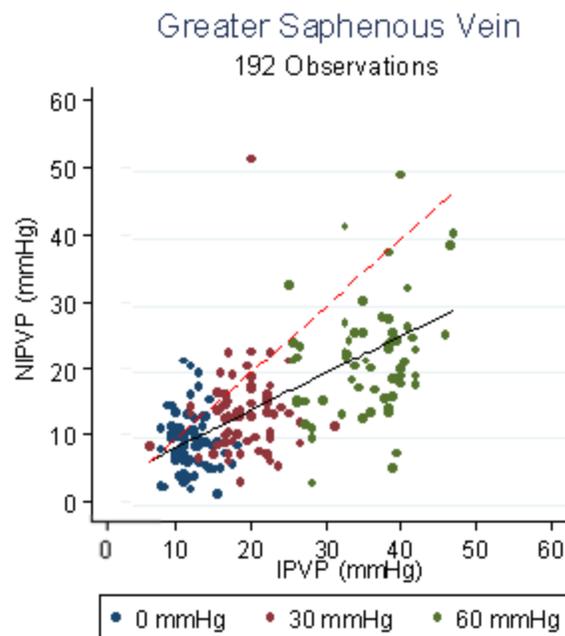


Figure 4. NIPVP vs. IPVP for the greater saphenous vein. Black line is estimated linear response to VP assuming IPVP has negligible error.

Jugular Vein

Pressure was not measured invasively in the jugular vein, but the NIPVP measurements were generally responsive to changes in tilt table angle (**Figure 5**) with some large outliers at the greatest tilt of 20°. Using mixed-model regression analysis with 4 outliers removed, we estimated a mean increase of 5.6 (95% conf. [4.2, 7.1]) mmHg in the non-invasive measure when θ increases from 0 to 10° and an increase of 11.3 (95% conf. [8.9, 13.6]) mmHg when θ increases from 0 to 20°. For this vein, there was no evidence of the operator ($p > 0.5$) or vertical distance from the heart ($p > 0.5$) affecting the NIPVP measurements in addition to the tilt angle. However, there was a general increase in these

measurements over the weeks of the study: 0.46 mmHg per week (95% conf. 0.22, 0.71; $p < 0.001$), suggesting that if IPVP had been measured, we also may have observed a decreased variability in NIPVP in comparison to IPVP measurements.

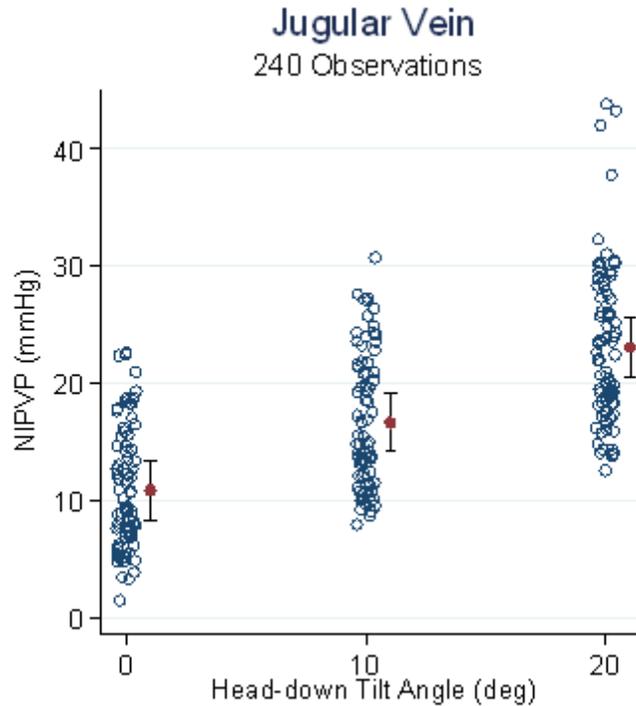


Figure 5. NIPVP vs. tilt table angle for the jugular vein. Open circles are individual data and the solid circles are the mean \pm 95% confidence interval. Actual tilt angles were 0, 10, and 20 degrees, but random horizontal scatter was introduced to make individual points more discernible.

Supratrochlear Vein

PVP was not measured invasively in the supratrochlear vein but was manipulated through changes in tilt angle as with the jugular vein. Day-to-day variation within subjects was too erratic to allow proper analysis of session-level data with a mixed regression model. Mixed-effects regression on the data collapsed over sessions showed that the combination of vertical site-to-heart distance (h) together with tilt angle (θ) proved to be a more important stimulus for the NIPVP measurements than tilt angle alone ($p = 0.001$). By contrast, changes in h had negligible effect on NIPVP measurements in the jugular vein. There was no evidence of an operator ($p = 0.85$) or a study week ($p = 0.35$) effect. The combined (θ, h) venous blood pressure PVP stimulus X estimated by the model was $C(\theta) - 0.16h$, where $C(\theta) = 2.25, 2.76, \text{ or } 3.48$ for $\theta = 0^\circ, 10^\circ, \text{ or } 20^\circ$, respectively. After estimating X , we re-plotted the session-level NIPVP measurements against X , rather than tilt angle to produce **Figure 6**.

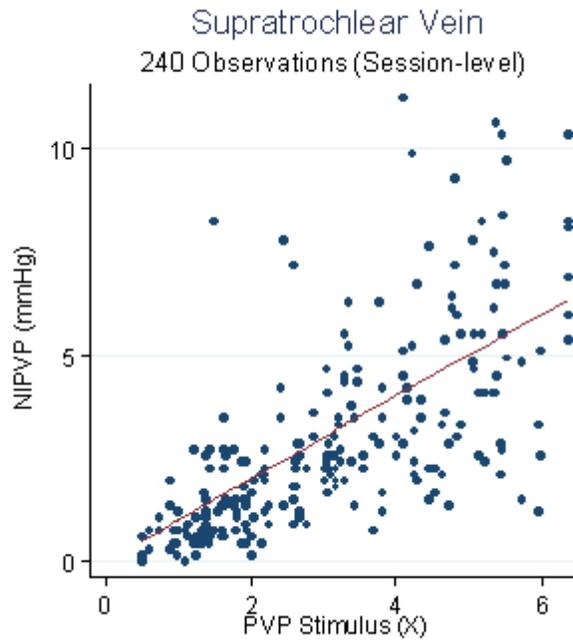


Figure 6. PVP stimulus (X), the combined effect of θ and h , plotted against NIPVP.

DISCUSSION

Our evaluation of the Vein Press prototype device has yielded several important findings which would influence future use of this device and interpretation of the measurements obtained. First, using this device, sonographers were able to measure increases in NIPVP in each of the veins studied in conditions expected to elevate venous pressure. Specifically, NIPVP measures increased from the baseline condition with increasing levels of venous occlusion in the cephalic and greater saphenous veins or head-down tilt angle in jugular and supratrochlear veins. Thus, the Vein Press prototype tested in this study may be a low-risk, non-invasive method of evaluating trends in venous pressures in response to various physiologic conditions, such as those seen in simulated or real microgravity.

Second, although the non-invasive PVP measures increased in the greater saphenous and cephalic veins when venous flow was partially occluded, the non-invasive PVP measures were significantly different than the invasive measures. The non-invasive PVP consistently underestimated the invasively measured venous pressure. A correction factor for non-invasive PVP obtained through statistical modeling might yield values which more closely match invasive measurements, but establishing such a correction factor was not part of this study. It is possible that this correction factor might require calibration within subjects due to variability between subjects in the amount and type of tissue overlying the vein of interest.

Third, the accuracy of non-invasive PVP improved as sonographers became more familiar with the device and the measurement technique, specifically in the cephalic vein. A portion of the increased accuracy might be attributed to increased experience with visualizing this relatively smaller vein; there was no evidence of a learning curve in measuring PVP in the larger greater saphenous vein.

Unfortunately, because we did not obtain invasive measures for the other veins studied, we could not extend these observations. We suspect, however, that the measurements obtained in the jugular vein are less likely to be influenced by learning due solely to its size. In contrast, as indicated by the large variability observed, we suspect that accurate measures in the supratrochlear vein are less likely and would require more extensive training and practice. Additionally, we observed that small deviations in the positioning of the ultrasound probe at the imaging site could produce inconsistent results, and we believe that more careful application of the VeinPress over the course of the time may have contributed to improved accuracy. With the experience obtained as a result of this study, we believe that we can institute improvements to the training of future Vein Press operators to reduce the time and amount of training required to obtain consistently accurate measures.

Fourth, despite undergoing similar training by a single instructor prior to the start of this study, there is the potential for different sonographers to obtain different measures of PVP, specifically in smaller veins. In our study, the NIPVP measurements of the cephalic vein obtained by one sonographer were different from those obtained by the other sonographer. We believe that these results are due in part to the size of the vein being measured. There were no between-operator differences for the two largest veins studied, the greater saphenous and jugular veins. We were unable to test for between sonographer differences in the supratrochlear vein due to the overall large variability in these measurements. Thus, due to the subjective nature of determining when a vein is compressed, especially in the case of smaller veins, it may be preferable for a single sonographer to perform all measurements for a single subject across the duration of a longitudinal or interventional study. As this may not always be feasible, further standardization of measurement techniques should be addressed to decrease the inter-sonographer measurement variability. Alternatively, researchers might consider limiting their studies to measuring PVP only in larger veins.

We believe, however, that the accuracy of the measurements, and perhaps inter-sonographer variability, can be improved with modification to the VeinPress. Specifically, we observed that imaging through the bladder of the VeinPress causes some degradation of the ultrasound image that increases the difficulty of reliably judging when the vessel is fully compressed. This problem is exacerbated with smaller veins, which are naturally more difficult to visualize. Image degradation impairs the ability to reliably judge vessel compression (already a subjective assessment), likely contributes to between and within sonographer errors, and thus impacts the overall quality of the PVP measurements. The supratrochlear vein was the smallest vein imaged, and the variability in the PVP measures for this vessel was the highest. The jugular vein was larger than the other veins imaged in this study and thus more readily visualized due to its size, leading to more consistent PVP measures across tilt angles. Therefore, the jugular vein may be a preferred location for NIPVP measures because of the lower impact of signal degradation. However, modifications in the bladder design from which the VeinPress prototype was constructed have been made since the completion of this study. This could potentially decrease the signal degradation so that smaller vessels could be more accurately and reliably measured in future studies.

Finally, it should be recognized that the VeinPress, while attractive for its simplicity, also by definition is strongly influenced by subjective nature of pressure application. The supratrochlear vein consistently had the lowest pressure readings across all tilt angles. This could point to a limitation of a hand held device to dependably measure pressures of less than 3 mmHg. It should also be noted that the device only reported measurements as whole numbers. Increases in supratrochlear vein pressure could

possibly have been more clearly delineated if the manometer displayed decimals. The fact that it only displayed whole numbers, in combination with very low venous pressure, suggests that it might not have reflected small incremental changes compared to the increased responses of the other higher pressure veins that we evaluated. Recording these measurements exclusively as a whole number could have led to our observation that the supratrochlear vein less sensitive to head-down tilt angle changes.

Limitations of the Study

We have identified three limitations of the study design which might have impacted the results of our pilot study and the applicability of our findings. First, the act of inserting a catheter within 5 cm of the imaging site for the cephalic and greater saphenous veins may have caused either a localized or sympathetic nervous system response to constrict the vein that could have influenced non-invasive venous pressure. We chose the close proximity between the catheter placement and the non-invasive measures to minimize the effects of measurement location on comparisons between invasive and non-invasive measures. However, during the stabilization period following the insertion of the catheter at each site, PVP measurements yielded dramatically high numbers compared to those that were observed by the end of the stabilization period, especially in subjects where catheter insertion was more difficult. Even though no data were recorded during the stabilization period, it is not clear whether there was any residual effect from the insertion following the stabilization period. If the physiological effect of catheter insertion does influence venous compression characteristics, this could explain some of the variability seen in the cephalic and greater saphenous veins. This situation could be addressed in future validations by instituting a longer stabilization period or by imaging further downstream of the catheter insertion site.

A second factor that could have influenced results of the more peripheral vessels was subject comfort and tolerance of room temperature (70°-75° F; 25.1°-23.8° C). The room was kept at a temperature that could be considered a comfortable working environment. When laying supine for over an hour, this same temperature can start to feel cool. We attempted to keep the core body temperature constant with the use of blankets and heating pads, however, it appeared that the sensation of cold was not noticed until after peripheral vessels have started contracting. This study was not designed to address whether a change in PVP was related to peripheral venoconstriction or temperature. The imaging of smaller vessels was more technically challenging and could lead to more variability, whether the size is related to constriction or not.

Third, although our data clearly demonstrate that the NIPVP measures in the cephalic and greater saphenous veins underestimate the values obtained by IPVP, it was not within the scope of this pilot study to develop a correction factor for these. Our results suggest that NIPVP measures are 2-3 times lower than those obtained by IPVP, but a larger number of subjects would be required to fully explore this relation, particularly since the expected IPVP may be small and the error involved in the NIPVP may be large in some subjects. Also, because the anatomical characteristics of the measurements site differ for each vein in this study, it is likely that a different correction factor will be required for each. Currently, we have no information on the relation between NIPVP and IPVP in the jugular and supratrochlear veins since IPVP was measured for these vessels.

CONCLUSIONS

Our experience suggests that while the prototype VeinPress 2010 device is potentially useful for the non-invasive assessment of peripheral venous pressure, factors contributing to the variability and accuracy of the non-invasive measurements should be further clarified prior to the routine use of the device clinically and in research applications. In particular, we have found that although there is a relationship between invasive and non-invasive measures of PVP, vessel size and operator experience can affect the results obtained. Since the completion of our pilot study, improvements in the design of the device have been made in the bladder, which may now yield results that more clearly match invasive measurements. This may be especially important in the study of smaller veins for which clear images are more difficult to obtain. Despite deviations of the non-invasive measures from those of invasive venous pressure, we have shown compression sonography has potential for the determination of venous pressure trends in selected veins and is more reliably obtained in larger vessels such as the jugular vein. The ability of the VeinPress prototype to reliably determine jugular venous pressure during different physiologic conditions is encouraging. The capability to observe changes in jugular venous pressure non-invasively on the International Space Station using the VeinPress will provide an ideal alternative to invasively detecting venous pressure changes that will prove insightful in NASA's endeavor to further understand the factors leading to increased intracranial pressure and the development of the Visual Impairment/Intracranial Pressure syndrome.

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