Hemodynamic physiology during perioperative intracranial hypertension
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Long-term pressure monitoring with arterial applanation tonometry: a non-invasive alternative during clinical intervention?

Modified from


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Abstract

**Background** : Arterial tonometry is a non-invasive technique for continuous registration of arterial pressure waveforms. This study aims to assess tonometric blood pressure recording (TBP) as an alternative for invasive long-term bedside monitoring.

**Methods** : A prospective study was set up where patients undergoing neurosurgical intervention were subjected to both invasive (IBP) and non-invasive (TBP) blood pressure monitoring during the entire procedure. A single-element tonometric pressure transducer was used to better investigate different inherent error sources of TBP measurement.

**Results** : A total of 5.7 hours of combined IBP and TBP were recorded from three patients. Although TBP performed fairly well as an alternative for IBP in steady state scenarios and some short-term variations, it could not detect relevant long-term pressure variations at all times.

**Discussion** : We discuss our findings compared to existing work and elaborate on why physiological alterations at the site of TBP measurement might be an important source of artifacts. We conclude that at this point arterial tonometry remains a too unreliable technique for long-term use during a delicate operative procedure and that physiological changes at the TBP measurement site deserve further investigation. Manufacturers of medical instrumentation should consider tonometry technology for long-term monitoring but the associated issues as presented in this work need to be resolved first.
Introduction

In previous work we reviewed the development and theoretical modelling of arterial applanation tonometry, a technique used for non-invasive and continuous measurement of blood pressure waveforms\(^1\). The tonometer is of particular use in clinical research studies concerning vessel wall compliance or arterial wave traveling. It allows for a ‘quick and easy’ recording over a few cardiac cycles of pressure waveforms at superficial arteries and such data facilitates the calculation of haemodynamical parameters that help characterize global vessel wall properties\(^1,2,16\).

It is remarkable that the tonometer has not been able to spread into daily diagnostic practice even though it is a simple, non-invasive device that allows for continuous blood pressure monitoring. Two areas immediately spring to mind where potential for a simple probe-based pressure measurement technique such as applanation tonometry might exist: (1) ambulatory pressure monitoring and (2) clinical bedside pressure monitoring.

Tonometry as an ambulatory blood pressure monitoring device could enhance the information of existing home ambulatory blood pressure recorders by adding beat-to-beat waveform information to the conventional single number output for systolic, diastolic and mean arterial pressure (SBP, DBP, MAP). But as commercial tonometric devices are all quite motion-sensitive, ambulatory monitoring might be a too challenging environment for now. However, in bedside monitoring during surgical procedures, the patient is supine and there is no direct need for ambulatory equipment. A vast amount of arterial line (A line) recording is performed as the arterial cannulation technique remains the accepted standard for long-term blood pressure monitoring in anaesthesia and critical care. Most commonly, radial artery pressure is registered because it is easy to perform and rarely associated with complications\(^10,14\), but despite the qualities of this technique, it remains an invasive technique with a substantial load for the patient.

The potential of long-term non-invasive monitoring with arterial applanation tonometry has not yet been fully explored. The ability to continuously and non-invasively monitor blood pressure in the operating room may be advantageous in a number of situations\(^8,9\), for example during induction or during surgical procedures where beat-to-beat measurements are essential but no blood samples are needed. Its indications could be expanded to any procedure where up to now only intermittent cuff monitoring is used.

The purpose was therefore to acquire combined invasive blood pressure (IBP) and non-invasive tonometric blood pressure (TBP) recordings during major neurosurgical operation. Using a single-element tonometric pressure transducer, we were able to capture unprocessed waveform data which allowed to investigate the effect of
different error-introducing aspects such as transducer fixation, positioning, calibration and recalibration which are difficult to assess with fully automated devices where positioning and a best signal is automatically chosen among the output of multiple transducer elements by means of an integrated software algorithm. Identifying and understanding the individual sources of error is imperative for developing liable pressure monitoring. As calibration of tonometric probes is most commonly performed with conventional sphygmomanometry and frequent recalibration is an important issue, the influence of cuff inflation proximal to the tonometric probe is also examined.
Methods

Set-up and measurement protocol

Data were measured in three patients, consecutively scheduled for major neurosurgical intervention. Written informed consent and institutional approval were obtained. Exclusion criteria were subclavian stenosis and pre-existing radial artery cannulation. Routine continuous monitoring in the operating room included electrocardiography, pulse oximetry, capnography, blood pressure recording and rectal temperature assessment. All patients remained in supine position. Patients were kept normothermic by a forced-air warming system.

General anaesthesia was induced by intravenous propofol 2 mg.kg$^{-1}$. Cis-atracurium 0.1 mg.kg$^{-1}$ was used for muscle relaxation. General anaesthesia was maintained by continuous infusion of propofol 6 mg.kg$^{-1}$.h$^{-1}$, remifentanil 0.1 $\mu$g.kg$^{-1}$.min$^{-1}$ and cis-atracurium 0.15 mg.kg$^{-1}$.h$^{-1}$. Patients were intubated orally and ventilated mechanically to achieve end-tidal CO$_2$ and oxygen saturation within normal limits. After anaesthesia induction, a 20-gauge 8cm PE catheter (Laeder Cath, Laboratoires pharmaceutiques, Ecouen, France) was inserted percutaneously into the left radial artery, 1 cm proximal to the wrist. The catheter was connected via a 150 cm long (1.5 mm internal diameter) rigid pressure tubing, filled with saline to a continuous flush pressure-transducer system (PMSET 1DT-XX Becton Dickinson Critical Care Systems Pte Ltd, Singapore). The system was calibrated against atmospheric pressure. The mid-axillary line was used as the zero-reference point.

At the contralateral arm, a single-element tonometric pressure transducer (model SSD-936, Millar Instruments, Houston, TX, USA) was placed over the right radial artery, about 1 cm proximal to the wrist.

Figure 1: Application Fixation of the tonometer.
Correct positioning was determined by palpation and waveform evaluation on the anaesthesia monitor. After locating the appropriate position, the transducer was immobilized by means of a Tegaderm™ patch (3M Health Care, Borken, Germany). Hold-down pressure was then adjusted by means of a custom made bracelet with screw until optimal waveforms with maximal amplitude were obtained. During the rest of the procedure, these settings remained unchanged.

All monitoring equipment was connected to an S5 monitor (Datex-Ohmeda, Helsinki, Finland). Because the Datex S5 monitoring system has no standard connection for tonometric probes, a custom connection was made for this study. Collecting all data via only one integrated monitoring and computing system has significant advantages (easy synchronisation of multiple signals, maximal patient-safety with minimal use of equipment). All data from the monitor were sampled via the Collect® Software (Datex-Ohmeda, Helsinki, Finland) package for subsequent off-line analysis. IBP and TBP waveforms were sampled at 100Hz. The total acquisition time for the first patient was 63 min, for the second patient 170 min and for the third patient 110 min.

Analysis

It is not an aim of this study to assess a particular tonometric device. Instead the focus lies on assessing general suitability of the tonometric technique for long-term monitoring. As such, the analysis is tailored towards answering the question: what can we observe clinically with the tonometric technique using the set-up described higher and how do trends in pressure changes compare to what is observed with the invasive standard. For it is pressure change trend behaviour that will trigger an action from the clinical observer in the operating room in the first place. Accurate trend agreement with IBP is therefore a minimal condition to be met by TBP.

Evaluation of normalized pressure waveforms

We investigated the trend behaviour of TBP and IBP recordings per acquisition window of 10,000 samples, avoiding the confounding influence of TBP calibration errors by normalizing both IBP and TBP signals to their respective first complete heart cycle in the acquisition window. The size of the acquisition window (10,000 samples) was based on the need for a workable time-interval (100s) that is small enough to be assessed adequately in one observation but still large enough to capture relevant pressure trends surrounding an event such as e.g. an external cuff inflation. Subsequently we differentiated the trends identified into four possible categories as distinguished by an experienced observer. These four categories are shown illustratively in Figure 2 (only a 20s time interval of a complete acquisition window of 100s is shown). The two vital cases are agreement (case A) or disagreement (case B) of the trends in the IBP and TBP signal: IBP and TBP can change in the same direction (case A-AGR); IBP and TBP can deviate in an opposite direction, or one signal deviates while the other stays in steady state (case B-DISAGR).
Two further cases were identified: both signals can be in steady state (case C-SS), and finally, poor TBP signal quality, no assessment of a trend possible (case D-ERR).

**Figure 2 : Four categories of trend behaviour of the tonometric signal.**

**Evaluation of calibration effects**
It is common practice to calibrate the tonometer with diastolic and mean pressure values from an oscillometric cuff\(^1\). However, it has been shown that an oscillometric recording can have a substantial error margin compared to direct invasive
recordings\textsuperscript{5,7,13}. Since in this study an invasive recording was performed concurrently with a tonometric recording, we decided to investigate the potential of applanation tonometry in the hypothetical case of having perfect calibration values available (as taken from IBP). This approach has also been applied in other work on tonometry\textsuperscript{4}.

However, in order to investigate the effect of external interference such as an inflating and deflating cuff on the recorded signal, we did apply an oscillometric brachial cuff at the same arm as the tonometric pressure transducer during several (randomly chosen) time intervals, recording systolic and diastolic blood pressure values every 3 or 5 min.

We also investigated the reliability of a calibration over time. In order to do this, we processed the acquisition windows in pairs, with a first and subsequent window. Note that the calibration analysis thus spans a double time interval (2 x 10,000 samples, or 200s for 100Hz) as compared to the trend analysis of the normalized signals. A set of waveforms with no obvious artifacts over a few heart cycles was chosen and averaged by the observer at the beginning of the first of each acquisition window pair. Calibration offset and gain values were assessed for this averaged TBP waveform using diastolic blood pressure (DBP) and mean blood pressure (MAP) values from the corresponding averaged IBP waveform. These calibration parameters were then applied on the whole acquisition window pair. Near the end of the second window, a second set of waveforms was chosen and averaged. For this second averaged waveform, the ratios between DBP, systolic blood pressure (SBP) and pulse pressure (PP) values of TBP and IBP were assessed, as well as the root mean square error (RMS) of their respective differences.

\section*{Results}

We obtained a total of 2,058,000 paired data points over a period of 343 minutes in 3 patients. Table 1 shows the evaluation of normalized TBP compared to normalized IBP by organizing the observed trend behaviour into four different categories as described higher (A-agree; B-Disagree; C-Steady state; D-Erroneous).

\begin{table}[h]
\centering
\caption{Qualitative evaluation of trends in TBP compared to IBP.}
\begin{tabular}{|c|c|c|c|}
\hline
{} & Acquisition Windows & \% of Total & \% of Subtotal \\
\hline
Total (A+B+C+D) & 282 & 100 & - \\
Subtotal (A+B) & 41 & 15 & 100 \\
Case A-Agree & 23 & 8 & 56 \\
Case B-Disagree & 18 & 7 & 44 \\
Case C-Steady State & 229 & 81 & - \\
Case D-Erroneous & 12 & 4 & - \\
\hline
\end{tabular}
\end{table}
From the total number (282) of acquisition windows investigated (A+B+C+D), only 4% showed poor signal quality of TBP. Further, 81% of all recordings were steady state scenarios and in this case TBP and IBP always had a very good correspondence. Since cases with signal variations are better markers than steady state cases on how the TBP and IBP agree, we focused on the subtotal (the remaining 15%) of cases in agreement or disagreement alone. For those two cases (A+B), the percentages are almost equally divided between A and B. Thus, in relation to the subtotal of windows in which pressure variations occurred, the TBP agreed with IBP only in 56%.

Figure 3: Illustration of the evolution of TBP readings related to IBP readings.
Investigating pressure variations in further detail, it appeared in all the subjects that small variations (e.g. caused by patient ventilation) were adequately followed by TBP (Figure 3A). Very fast changes such as an extra-systolic event are also adequately captured (Figure 3B & C). However, the more the pressure change is longer in time or higher in amplitude, the more TBP monitoring tends to stay invariant to these pressure changes (Figure 3D).

Next, calibration of TBP was performed. Note that the acquisition windows categorized higher are now analysed in pairs as explained in the methods section. From a total of 141 pairs, 2 had a too poor signal quality to be included in the results. An analysis of differences between TBP and IBP (calibration precision) was performed on the remaining 139 acquisition window pairs (with each window consisting of 10,000 data points). Overall agreement (point-by-point) between TBP and IBP yielded an average RMS value of $31.3 \pm 12.1$ mmHg among the three patients, while the RMS for SBP, DBP and PP values resulted in $18.3 \pm 9.3$ mmHg, $12.1 \pm 4.4$ mmHg and $11.0 \pm 5.6$ mmHg respectively. Considering the data of all patients together, we found an RMS of $34.3$ mmHg for overall agreement and an RMS of $20.8$ mmHg for SBP, $13.2$ mmHg for DBP and $12.2$ mmHg for PP.

Further, the ratios of SBP, DBP and PP between TBP and IBP are represented in Table 2 and Figure 4.

Table 2 shows the number of acquisition window pairs for which Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Pulse Pressure (PP) from calibrated Tonometric Blood Pressure (TBP) lie within the 5% and 10% discrepancy intervals of the respective SBP, DBP and PP from Invasive Blood Pressure (IBP), and this for all patients together.

<table>
<thead>
<tr>
<th>Total = 139 Acquisition Window Pairs</th>
<th>TBP &lt; IBP ± 5%</th>
<th>TBP &lt; IBP ± 10%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># Pairs</td>
<td>% of Total</td>
</tr>
<tr>
<td>SBP</td>
<td>54</td>
<td>40</td>
</tr>
<tr>
<td>DBP</td>
<td>43</td>
<td>31</td>
</tr>
<tr>
<td>PP</td>
<td>45</td>
<td>32</td>
</tr>
</tbody>
</table>
Figure 4 shows the number of pairs of acquisition windows (# pairs AWin) vs. ratio (%) of Systolic Blood Pressure, Diastolic Blood Pressure and Pulse Pressure values from Invasive Blood Pressure (I-SBP; I-DBP; I-PP) and the respective values from calibrated Tonometric Blood Pressure (T-SBP; T-DBP; T-PP) for all patients together. Note that the # pairs AWin in e.g. a 5% discrepancy interval (as mentioned in Table 2) are found on these plots by adding the bars in both the 95-100% (minus 5%) and 100-105% (plus 5%) interval.

**Figure 4 : Distribution of the disagreement between TBP and IBP measurement.**

A value of 110% means that the IBP value is 10% higher than the TBP value. From these data it is clear that when looking at the three patients together, 38.8% of SBP values, 30.9% of DBP values and 32.4% of PP values from calibrated TBP are within ±5% of IBP. Also, 63.3% of SBP, 55.4% of DBP and 53.2% of PP values lie within the ±10% discrepancy interval. Given the fairly equal distributions in Figure 4 around 100%, there is no evidence of a consistent over- or underestimating (calibration bias) by TBP recordings. However, considering only the very large deviations (more than ±25%), we did note more cases of underestimation (IBP/TBP > 125%) than overestimation (IBP/TBP < 75%) by TBP, and this for SBP as well as for DBP and PP.
Discussion

In summary, TBP was recorded with IBP for 5.7 hours during neurosurgery. Thus, despite the small number of patients that did not allow for an inter-subject variability study, we did obtain a large set of waveform data for overall comparison of IBP and TBP. Our findings showed that calibrated TBP mirrored IBP adequately in all steady state conditions and that minute variations of blood pressure e.g. caused by patient ventilation or very short variations such as an extra-systolic wave were well detected. However, these kind of variations are usually of no clinical relevance unless in specific studies. For pressure variations longer in time and with high amplitude, there was a rather high degree of unpredictability. In nearly half of the investigated acquisition windows TBP either deviated in the opposite way or was only adequately following IBP in the first seconds after a pressure change to then untruly return to its initial regime suggesting a steady state, while IBP continued to vary.

Our set-up consisted of a single-element tonometric transducer set-up, without automated feedback and control for position and hold-down pressure, deprived of advanced signal conditioning and using ideal calibration values as taken from IBP. As such stripped from possible confounding factors, our findings still indicated inaccurate trend behaviour, suggesting that the technique of TBP monitoring is for now unreliable or not enough understood at best to replace IBP monitoring in a clinical setting. This mere statement alone is not an entirely new result, and two other studies with related findings are addressed below. In analogy with our theoretical review, we aimed however with this practical work to add on the existing knowledge by not merely dismissing the technique as unsuitable but rather to assess how tonometry has evolved (or not) since past efforts, and to add (physiological) insights into its associated problems which have not been clearly investigated before.

A decade ago Weiss and colleagues concluded from short-term recordings using an automated multi-element array transducer (SA-250, Colin, Komaki, Japan) that tonometry was not suitable to replace invasive monitoring during major surgical procedures. However, we demonstrated here with a simple (more controllable) set-up of a single-element transducer and a custom fixation mechanism, that short-term variations can be detected reasonably well. First, this discrepancy may well be attributed to the evolution in transducer sensitivity over the years. Second, tonometer positioning, signal calibration and signal display in automated devices are assessed not by the operator but by an integrated software algorithm choosing a best output signal among multiple elements of the transducer in the tonometric device. This is a limitation when looking into causes of signal artifacts and variations, hence why in this study we chose a single-element tonometric pressure transducer, put in place by the operator with precision so that unprocessed data could be displayed and recorded from a well-known location to facilitate the later analysis of signals and artifacts.
Non-invasive continuous pressure monitoring

More recent work of Steiner and colleagues in a neuro-intensive care setting also used a fully automated tonometry device (CBM-7000, Colin Medical, San Antonio, TX, USA) and did perform long-term recordings (60 min)\(^\text{15}\). It was concluded that the tonometric device was not accurate enough for replacing invasive blood pressure (IBP) monitoring because of the significant number of inaccurate measurements and a downward signal drift. Although the quantitative analysis for comparing TBP with IBP was commendable, the underlying causes of the inaccuracies and drift were not further examined.

Apart from movement artifacts, positioning and fixation of which the influence on signal quality was described in earlier work\(^\text{6,11}\), the problems are mainly caused by the dependence of the tonometer from an external calibration device, usually a brachial cuff-measurement based on oscillometry, of which the intrinsic restrictions have their repercussions on the tonometric signal accuracy\(^3\). The drift noticed by Steiner and colleagues in the time following recalibration may well be the result of physiological changes in the limb distal to the inflated cuff.

To demonstrate this hypothesis, we applied a varying external force on the arm by means of a brachial cuff and thus artificially induced a clear and reproducible blood pressure change. We looked at the pattern of the uncalibrated TBP during inflation and release of the cuff, as would occur when the calibration cuff would be positioned at the same arm as the tonometer. By capturing the unprocessed pressure waveforms with the single-element tonometric pressure transducer, we were able to elaborate on the physiological changes induced by cuff inflation.

When taking a close look at TBP waveforms during cuff inflation, different events can be distinguished that are observed repeatedly and systematically after every cuff inflation.

**Figure 5 : Pattern of the TBP reading during cuff inflation and deflation.**
We speculate that the induced physiological phenomenon can be explained as follows: after the initial cuff inflation, venous pressure starts to increase, while arterial pressure distal to the cuff doesn’t change appreciably. One can observe that MAP of TBP increases significantly, while PP diminishes only modestly. This could be explained by venous stasis causing the rigid hold-down bracelet to tighten slightly, which in turn delivers a significant increase of hold-down force onto the small pressure transducer element so that it demonstrates an increased pressure.

Once the cuff is inflated to maximum level, one can see that PP of TBP drops to zero, while MAP of TBP stagnates. This is logical since total occlusion of the artery and veins implicates that no blood can flow in or out. After this, the cuff is deflated slowly in order to detect SBP and DBP by means of oscillometry. Once the cuff is deflated below the SBP, one can see MAP and PP of the TBP signal rising quickly to a new plateau. This plateau might correspond to maximal venous stasis when venous pressure approximates arterial pressure. Possibly, since the cuff inflation caused an ischaemic stimulus to the smooth muscle cells in the distal arterial vessel walls, the vessels may dilate and increase the force onto the tonometric pressure transducer. At this point, the cuff pressure is between SBP and DBP. Once the cuff pressure is further released and drops below the venous pressure, the TBP returns towards its normal values remarkably fast, which suggests indeed a predominantly intravascular cause of the artifact. Note that although almost completely restored to the normal values at this point, it actually takes another minute of slow but steady recovery to really get to the initial baseline (not shown). It is unclear whether the latter would mean that extravascular physiological disturbances play a secondary role, but it is in any case obvious that a signal disturbance has a prolonged effect that is not negligible compared to the conventional time span for recalibration (around 3-5 minutes for hand-held as well as automated devices).

**Conclusion**

A practical study was presented in a challenging clinical setting in which we evaluated the proof of concept of long-term radial artery pressure waveform monitoring via non-invasive applanation tonometry, and this as an alternative for invasive blood pressure measurement via radial artery cannulation. We analysed long-term recordings in three patients undergoing neurosurgery. Differently from other work, we used a single-element tonometric pressure transducer to control and investigate the different error-introducing aspects and we also elaborated on the possible underlying physiological influences in the lower limb during tonometric recording and oscillometric cuff calibration.

We conclude that, in this patient study and the tested setting, the tonometric pressure transducer was not able to detect the relevant pressure changes at all times and a rather high degree of unpredictability was present. As such, we believe that arterial
Non-invasive continuous pressure monitoring

tonometry still remains an essentially unreliable technique for use during a delicate operative procedure. As we discussed, physiological alterations at the site of tonometric measurement can be an important source of artifacts and further study of the source of these artifacts is essential for reliable long-term non-invasive assessment of blood pressure via applanation tonometry.

Tonometry technology represents only a small niche with respect to the blood pressure-monitoring field. Globalisation has forced some devices of the market and new initiatives face difficulties in taking off beyond the prototype stage. Incorporation in cardiovascular profiling systems (e.g. the Sphygmocor® Technology from Atcor Medical or the CVProfilor® from Hypertension Diagnostics) is the norm. Bedside and ambulatory pressure monitoring can present new opportunities for manufacturers of tonometric devices, provided they tackle the persistent issues associated with long-term recording as highlighted in this work.

References
