Aneurysm sac pressure monitoring: Does the direction of pressure measurement matter in fibrinous thrombus?


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Abstract

**Objective:** To clarify the effect of the direction of pressure measurement on the pressure read-out in fibrinous thrombus.

**Methods:** Three weights of 468g (1), 578g (2) and 675g (3) were molded. A specimen of human fibrinous thrombus was positioned under the weights. Since the surface area of the weights and the thrombus was 400mm², weights 1, 2 and 3 caused a pressure of 88 mmHg, 108 mmHg and 127 mmHg, respectively. Pressure measurements were performed at different angles between the sensor and the applied force (0°, 22.5°, 30°, 45°, 60°, 67.5°, 90°). Thrombi of ten different patients were analyzed. Pressure measurements in the thrombi at different angles were statistically compared by a Linear Mixed Model analysis.

**Results:** The measurements at 90° differed statistically from the measurements at 0°, 22.5°, 30°, 45°, 60°, and 67.5° (p < 0.001). The pressure read-out was only similar to the applied pressure when the pressure sensor was positioned at a right angle to the applied force. Pressure measurements in other sensor positions resulted in lower pressure measurements. Pressure changes were detected in all sensor positions. There appeared to be no significant difference between the pressure measurements taken at same angles in the ten thrombi (p > 0.05).

**Conclusion:** In fibrinous thrombus, the direction of pressure measurement influenced the pressure read-out.
8.1 Introduction

The purpose of endovascular aneurysm repair (EVAR) is preventing the abdominal aortic aneurysm (AAA) from rupture by depressurizing the aneurysm sac. An important complication of EVAR is the occurrence of endoleaks and endotension. Endoleak, an incomplete seal of the aneurysm sac and endotension, an increase in aneurysm diameter without detectable endoleak, are associated with increased aneurysm sac pressures [1]. Hence follow-up after EVAR is needed to detect endoleak and endotension. Since aneurysm sac pressure is directly related to the aneurysm rupture, there is a great interest in aneurysm sac pressure monitoring [2]. Direct aneurysm sac pressure measurement could be a valuable tool during the follow-up after EVAR [3]. Unfortunately, aneurysm sac pressure monitoring is not straightforward [4–6].

The sensor position in fluids is not relevant for pressure measurement, because the forces at a given point in a fluid are identical in all directions. This is not the case in solid materials [2]. Since the aneurysm sac is filled with solid fibrinous thrombus, aneurysm sac pressure measurement could be hampered. The aim of this study was to investigate the effect of the direction of the pressure measurement on the measured pressure level in fibrinous thrombus.

8.2 Methods

8.2.1 Experimental set-up

The experimental set-up is depicted in Figure 8.1 and 8.2. The set-up consisted of a table (A) with holder (21 × 21 × 40 mm) (B). Three weights (C) of 468g (20 × 20 × 115mm) (1), 578g (20 × 20 × 145mm) (2) and 675g (20 × 20 × 160mm) (3) were molded. The weights fitted exactly in vertical position in the holder, to position the weights at right angles to the tabletop (Figure 8.1). The surface area between the weights and the tabletop was 400mm$^2$ (20 × 20mm). Therefore, the pressure caused by the weights can be calculated with the following formulas:

$$F = m \times g$$

(8.1)

$$P = \frac{F}{A}$$

(8.2)

where $F$ is the force in N/m$^2$, $g$ is the gravity 9.81 in m/s$^2$, $P$ is the pressure in N/m$^2$, and $A$ is the area in m$^2$. To convert pressure from N/m$^2$ into mmHg, the result is multiplied by the constant $7.502 \times 10^{-3}$. Weights 1, 2 and 3 cause a pressure of 88 mmHg, 108 mmHg and 127 mmHg, respectively.

6 holes were computer-controlled drilled in the tabletop, under calibrated angles of 0°, 22.5°, 30°, 45°, 60° and 67.5°, respectively (Figure 8.1). The holes
were positioned in such a manner that the axes of the holes intersect at 7.5 mm above the table (Figure 8.1).

### 8.2.2 Pressure sensors

A previous study demonstrated that fluid-filled pressure devices inserted into media like human fibrin thrombus do not yield accurate and reproducible results [4]. Catheters with tip-sensors are considered the gold standard for aneurysm sac pressure measurements [7].

During this study a pressure catheter with tip-sensor (RADIAnalyzer PressureWire Sensor®, RADI Medical Systems AB, Uppsala, Sweden) was used. This commercially available coronary PressureWire has a 3-cm long radiopaque platinum floppy tip. The radiopaque tip was snipped off distal to the sensor to enable precise positioning of the sensor. According to the manufacturer shortening of the radiopaque tip does not influence the accuracy of the sensor. The pressure sensor had a pressure sensitivity of 5.0 \( \mu \text{V/V/mmHg} \), corresponding to an accuracy better than 2 mmHg and a frequency response of 0-25 Hz or higher.

### 8.2.3 Experiments

Fibrinous aneurysm sac thrombus of ten patients was obtained during open aneurysm surgery. The thrombi were cut in parallelepipeds \((20 \times 20 \times 15\text{mm})\). The samples were kept wet by immersion in saline solution 0.9%.

7 needles (21G) were inserted in the holes in the tabletop to determine the distance between the intersection of the needles (7.5 mm above the table) and the underside of the table (Figure 8.1). The needles were marked to be sure that the tip of the needle was exactly positioned in this intersection. Finally, all needles were removed.

Subsequently, the first sample was positioned straight under weight 2 (Figure 8.1). The thrombus was punctured with a 21G needle from below the tabletop through the calibrated hole \((0^\circ)\) in the tabletop. The depth of puncture was determined using the marking on the needle. Before pressure sensor insertion, the sensor was calibrated in saline solution. The pressure catheter was inserted through the needle in the thrombus. The sensing element of the pressure catheter was situated on the side of the catheter and was always oriented upwards (Figure 8.1 and 8.2). We checked this during control experiments by cutting the thrombus after sensor introduction (Figure 8.2). These experiments confirmed that the sensor does not rotate after introduction in the thrombus. If the sensor was oriented upwards before introduction it was also positioned upwards after introduction.

Pressure measurement was performed one minute after withdrawal of the needle over the pressure catheter. Subsequently, weight 2 was removed and replaced by weight 1 and 3, respectively. Pressure measurements were repeated.
The pressure measurements were considered valid when the pressure readout after removal of the weight was within 5 mmHg of the expected 0 mmHg (atmospheric pressure). This check was performed to exclude artifacts caused by pre-stress on the sensor due to sensor introduction [5].

The same procedure was repeated after puncturing the thrombus through hole 22.5°, 30°, 45°, 60° and 67.5°, respectively. Pressure measurements at 90° were performed by horizontal insertion of pressure catheter in the thrombus parallel to the table-top. Pressure measurements at all angles were taken at exactly the same location in the thrombus.

Finally, the other 5 thrombus samples were punctured vice versa. First pressure measurements were performed at 90°, subsequently at 67.5°, 60°, 45°, 30°, 22.5° and 0°.

8.2.4 Statistical analysis

The pressure measurements at different angles were compared statistically by means of a Linear Mixed Model to evaluate the effect of the direction of pressure measurement on the pressure read-out in fibrinous thrombus.

The reason for using this analysis is that some factors can be considered as fixed effects and some as random effects. The effect of the angle of pressure measurement and the effect of the weight on the pressure measurements are fixed effects. The effect of the thrombus on the pressure measurement is a random effect, because we were not especially interested in the sample itself. The thrombus samples were considered as a reflection of the thrombi of patients with an AAA. Statistical significance was defined as a $p$-value of < 0.05. For statistical analysis, SPSS 12.0 for Windows was used (SPSS Inc, Chicago, USA).

8.3 Results

All pressure measurements of this study are depicted in Figure 2. A positive correlation between the angle and the pressure-read out was observed during all experiments since an increase in the angle of pressure measurement resulted in an increase of pressure read-out (Figure 8.3).

The pressure read-out was only similar to the applied pressure when the pressure sensor was positioned at right angles to the applied force. Pressure measurements in other sensor positions resulted in lower pressure read-outs.

The pressure measurements at 0°, 22.5°, 30°, 45°, 60° and 67.5° differed statistically significant from the pressure measurement at 90° ($p < 0.001$). The difference between pressure measurements in the ten thrombus samples at the same angle of measurement was not statistically significant ($p > 0.05$).

Pressure changes were detected by the sensor, independent of its position, after changing the applied pressures (Figure 8.3).


**Figure 8.1:** The experimental set-up consisted of a table (A) with holder (B) to position the weights (C) at a right angle to the specimen of human fibrinous thrombus (D). 7 needles are positioned in the calibrated holes. The intersection of the needles was 7.5 mm above the tabletop. $\alpha$ is the angle between the applied force and the sensor.

### 8.4 Discussion

In this study the direction of the applied force in relation to the sensor influences the pressure measurement in fibrinous thrombus. Pressure measurements in fibrinous thrombus were only similar to the applied pressure if the pressure sensor was positioned at a right angle to the applied force.

The results can probably be explained by the fact that the thrombus is a fibrinous media with certain porosity. Electron microscopy images of aneurysm sac thrombus demonstrated a structure of fibrin fibers [8] such that the static fluid pressure is present in the pores of this structure. The inter-fiber distance in the thrombus is a few micrometers [8], whereas the piezoelectric sensing element of
Figure 8.2: A piece of thrombus has been cut to check the sensor position after insertion. The sensor did not rotate after insertion. Measurements were always performed with the sensor in upwards position.

Figure 8.3: Pressure measurements in ten thrombi (mean ± SEM) after changing the weights (applied pressure). Measurements are performed at different angles between the sensor and the applied force.

The pressure catheter has a measurement area of $1.8 \times 0.36$ mm. Therefore, the sensor will measure a combination of hydrostatic fluid pressure and stress related to the solid fibrinous media. If the sensor is positioned at a right angle to the applied force ($90^\circ$), the weights create a stress field on the sensor equal to the applied pressure. Therefore, the stress in the solid material and the hydrostatic pressure of the fluid enclosed in the pores are equal to the applied pressure. The pressure sensor will measure a pressure similar to the pressure applied on the sample. If the sensor is positioned at 0 to the applied force, the sensor will measure a lower pressure since the part of the sensors that is in contact with the fibers hardly
experiences solid stresses. The sensor will only sense the hydrostatic pressure.

During the present study we demonstrated that the force at the place of measurement was different in different directions. Different forces on the membrane of the RADI PressureWire, in which the piezoelectric sensor has been incorporated, result in different pressure readings. This phenomenon has already been discussed in theory [2]. Since the problem of pressure measurement in thrombus is not caused by the sensor itself but by the different stresses and pressures in different directions, it is unlikely that the findings of this study are specific for the RADI PressureWire and could therefore be extrapolated to other sensors.

Pressure measurements were taken at the same location. Theoretically, the thrombus matrix could be damaged with each needle insertion. If the matrix is damaged, then more fluid may gather at this location with each needle insertion. Experiments could be biased because if more fluid is gathered at the location of measurement, the fluid pressure plays a more important role than the stress related to the solid fibrinous media. This could lead to falsely equal pressure readings in the subsequent measurements, since pressure in fluids is measured irrespective of direction of force. Therefore, measurements were taken from 0 degrees to 90 degrees as well as from 90 degrees to 0 degrees. In the present study we demonstrated that the sequence in which the pressure measurements were taken did not influence the outcome. The results were reproducible despite reversal of the order of measurements. It is therefore not likely that the findings of this study have been biased by a possible damage of thrombus matrix. During both orders of measurements the pressure measurements were only similar to the applied pressure if the pressure sensor was positioned at a right angle to the applied force. Pressure measurements in different thrombi at identical angles did not differ significantly from each other. This confirms the reproducibility of the pressure measurements in this study.

We appreciate that our experimental set-up is a simplified simulation of the in-vivo situation. This experimental set-up was developed to determine the effect of the direction of pressure measurement in fibrinous thrombus on the pressure-read out. However, using this set-up it is possible to position the sensor exactly at the same location in the thrombus (intersection at 7.5 mm above the table) and to measure at validated angles. An in vivo measurement of this kind will be very difficult, because exact determination of the angle between the endoleak and the pressure sensor is impossible.

Much research has been undertaken to evaluate aneurysm sac pressure after EVAR. Dias et al. measured a mean pressure index (MPI), the ratio between the mean aneurysm sac pressure and the mean systemic pressure, in patients with shrinking, stable and expanding aneurysms after EVAR. They concluded that intraneurysm sac pressure measurement is an important adjunctive for EVAR evaluation, because high pressure was associated with AAA expansion and low pressure with shrinkage [9]. However, it will be difficult if not impossible to determine a
definitive pressure threshold for intervention because the angle between the endoleak and the sensor is unknown during translumbar puncture of the aneurysm sac. Furthermore, it is uncertain whether the angle between the endoleak and the sensor is similar during two consecutive translumbar punctures. Therefore, monitoring the pressure trend of the aneurysm sac will be hampered.

Ellozy et al. reported the first clinical experience with the use of permanently implantable wireless pressure sensors to monitor the aneurysm sac pressure after EVAR [10, 11]. The optimal position of a wireless pressure sensor is not clear. The main problem is that the location of a possible endoleak is unknown before a wireless pressure sensor is positioned in the aneurysm sac. Hence the angle between the endoleak and the sensor is unknown. Therefore, it will be difficult to accurately measure pressure in the aneurysm sac. However, in the present study we demonstrated that pressure changes will be detected irrespective of the sensor position (Figure 8.3). If wireless pressure sensors remain in same position, a pressure trend after EVAR is probably most appropriate to follow. This corresponds with findings of our previous study [5].

In conclusion, our study demonstrates that the direction of pressure measurement in fibrinous thrombus influences the pressure read-out. Pressure measurements in fibrinous thrombus were only similar to the applied pressure if the pressure sensor was positioned at a right angle to the applied force. Pressure change was linearly detected, irrespective of direction of measurement. Therefore, a pressure trend seems more appropriate to follow than the absolute intrasac pressure. Further research is necessary to elucidate the pitfalls of aneurysm sac pressure monitoring and to determine the clinical relevance of aneurysm sac pressure monitoring after EVAR.

Acknowledgement

We thank Mr. M. Boonekamp jr. and his colleagues of the Department of Research and Development LUMC for their contribution to the construction of the experimental set-up and Mr. R. Wolterbeek, MD DipStatNSS, Statistical Consultant, Department of Medical Statistics LUMC for his advice in the statistical analysis.
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