

How much of the intra-aortic balloon volume is displaced towards the coronary circulation?

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Running head: Volume displacement during IABP

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Abstract

Objective: During Intra-Aortic Balloon (IAB) inflation, blood volume is displaced towards the heart (V_{tip}), traveling retrograde in the descending aorta, passing by the arch vessels, reaching the aortic root (V_{root}) and eventually perfusing the coronary circulation (V_{cor}). V_{cor} leads to coronary flow augmentation, one of the main benefits of IAB pumping. The aim of this study was to assess V_{root} and V_{cor} *in vivo* and *in vitro*, respectively.

Methods: During IAB inflation, V_{root} was obtained by integrating over time the aortic root flow signals measured in 10 patients with IAB assistance frequency 1:1 and 1:2. In a mock circulation system, flow measurements were recorded simultaneously upstream the IAB tip and at each of the arch and coronary branches of a silicone aorta during 1:1 and 1:2 IAB support. Integration over time of the flow signals during inflation yielded V_{cor} and the distribution of V_{tip} .

Results: In patients, V_{root} was $6.4 \pm 4.8\%$ of the IAB volume during 1:1 and $10.0 \pm 5.0\%$ during 1:2. *In vitro* and with an artificial heart simulating the native heart, V_{cor} was smaller, 3.7% and 3.8%, respectively. The distribution of V_{tip} *in vitro* varied, with less volume displaced towards the arch and coronary branches and more volume stored in the compliant aortic wall when the artificial heart was not operating.

Conclusions: The blood volume displaced towards the coronary circulation due to IAB inflation is a small percentage of the nominal IAB volume. Although small, this percentage is still a significant fraction of baseline coronary flow.

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Ultramini-Abstract

The blood volume displaced towards the coronary circulation during Intra-Aortic Balloon (IAB) inflation was assessed *in vivo* and *in vitro*. This volume was approximately 5% of the nominal volume of the IAB. Although small, this volume can provide significant augmentation in baseline coronary flow.

Word count: 44

Introduction

The Intra-Aortic Balloon Pump (IABP) provides mechanical support to the heart, both in the surgical setting pre-, post- and intra-operatively and in the medical setting in clinical conditions such as cardiogenic shock, myocardial infarction or unstable angina (1-5). It is also often used as a bridge to cardiac transplantation (4, 6).

The balloon (IAB) starts to inflate immediately after left ventricular (LV) ejection and completes deflation before the onset of the following LV ejection. Accurate timing is essential for optimum IABP performance.

When the IAB is inflated it displaces blood volume upstream, towards the heart, producing an increase in early-diastolic aortic pressure and providing a boost to coronary blood supply. Similarly, when the IAB is deflated it draws blood volume downstream, away from the heart, reducing end-diastolic aortic pressure and thus LV afterload. Other beneficial effects related to these major outcomes are decrease in LV volume and LV systolic work, reduction in end-diastolic and peak-systolic aortic pressure, increased stroke volume and improved cardiac output (4).

In this study we focused on the phase of IAB inflation and more specifically on the blood volume displaced towards the coronary circulation during inflation. *In vivo* studies report increased peak diastolic and mean coronary flow velocity, and increased diastolic coronary flow velocity integral in healthy coronary vessels (3, 7-10), but reports on the blood volume flowing through the coronary arteries due to inflation (V_{cor}) are scarce. A microsphere study in sheep reports V_{cor} of 0.1 ml/min/g in myocardial tissue supplied by a non-stenotic artery (11), but there are no comparable data in humans.

The IAB is placed in the descending aorta, between the arch vessels and the renal arteries. During IAB inflation blood volume is displaced upstream the IAB tip (V_{tip}), travels retrograde in the descending aorta, passes by the arch vessels, travels into the ascending aorta, arrives at the aortic root (V_{root}) and eventually is directed into the coronary circulation as V_{cor} . Neither V_{root} or V_{cor} nor their relation to V_{tip} is adequately reported in the literature. Accordingly, the aim of this study is to measure V_{root} in humans, as an indication of the volume pushed towards the coronary arteries due to IAB inflation. A more detailed *in vitro* study in a mock circulation was also conducted, where the

distribution of V_{tip} in the aortic arch, the coronary branches and the compliant aortic wall was quantified.

Methods

In vivo data

The study population consisted of 10 patients (7 males; mean age 56 ± 5 yr) who were supported by the IABP at least two days prior open-chest surgery for VAD placement. The protocol was approved by the Human Subjects Protection Program Office of the University of Louisville and written informed consent was obtained from all patients.

IAB catheters (Datascope, NJ, USA) with a balloon size of 34 or 40 cc were inserted via the femoral artery and connected to the IABP (System 98 or CS100, Datascope).

The patients were anaesthetized according to a routine protocol and anaesthesia was maintained with Isoflurane.

Simultaneous aortic (P_{ao}) and left ventricular (P_{LV}) pressure signals were recorded with a high fidelity 5F dual-pressure-sensor catheter (Millar Instruments, TX, USA). Flow (Q_{ao}) was measured at the same location as P_{ao} with a perivascular flow probe (Transonic Systems Inc, NY, USA). P_{ao} and Q_{ao} were obtained at the aortic root, distal to the coronary arteries. Hemodynamic data and the ECG were recorded at 200 or 400Hz.

In all patients, data were recorded prior to VAD placement with IABP assistance frequency of 1:1, 1:2 and also when the pump was on standby. Timing of inflation and deflation was based on the aortic pressure signal recorded internally by the pump with the fluid-filled catheter incorporated in the IAB. For each pump setting, data were collected continuously for approximately 15 s and a few minutes were allowed between successive measurements for hemodynamics to stabilize.

For each patient a single representative beat was selected for each condition. Figure 1 shows typical examples of P_{ao} and Q_{ao} recordings during a control and its following assisted beat from a 63 (Figure 1A) and a 60 yr old male patient (Figure 1B). As can be deduced from the onset of the rapid increase in P_{ao} during early-diastole with respect to the incisura, Figure 1A corresponds to a case of well-timed inflation, whereas Figure 1B illustrates a case of fortuitous late inflation.

From the aortic root flow measurements, V_{root} was calculated by integrating over time the negative peak during IAB inflation, as shown in Figure 1. V_{root} was normalized with respect to IAB volume, in order to render results between patients assisted with different IAB sizes, comparable.

Averages per beat were calculated for P_{ao} , Q_{ao} and systolic P_{LV} .

In vitro data

A physiological distribution of resistance and compliance was applied across a silicone aortic model (Ranier, Cambridge, UK) with 14 main branches (left and right coronary, left and right carotid, left and right subclavian, celiac, splenic, left and right renal, left and right femoral, and left and right deep femoral). Realistic values for terminal resistance and compliance of each branch were obtained from the model described by Stergiopoulos et al. (12), after reducing their 55-branch model to 14 branches by summing resistances and compliances according to basic *in parallel* and *in series* electrical circuit concepts. Flow out of each branch was directed to a common drainage tube and was connected to an overhead water reservoir providing a head pressure of 10 mm Hg in the silicone model.

An extracorporeal left ventricular assist device (BVS5000, Abiomed Inc, MA, USA) was used to simulate the native heart *in vitro*. It was driven with water by a piston pump (Placepower, Norfolk, UK) and provided a cardiac output of 2.7 l/min at a heart rate of 60 bpm, working close to its maximum capacity. The ‘left ventricle’ of the artificial heart was connected to the ‘aortic root’ of the aortic model and the ‘left atrium’ to the overhead reservoir. The IABP was triggered by the piston pump.

Intra-aortic balloons (Datascope) with size of 25 and 40 cc were inserted via the ‘left common femoral’ branch, advanced into the aorta until their tips were just distal to the subclavian branch and connected to the IABP (System 97e, Datascope).

‘Aortic’ pressure (P_{tip}) at the tip of the IAB was recorded with a solid-state 7F sensor-tipped catheter (Gaeltec Ltd, Isle of Skye, UK). Flows (Q) at the tip of the IAB (Q_{tip}) and through the ‘carotid’, ‘subclavian’ and ‘coronary’ branches were measured with 20, 10, 8 and 3 mm flowprobes respectively (Transonic Systems Inc). Data were digitized and recorded at 500Hz using a LabView-based acquisition system.

In order to assess the effect of the IAB inflation separately from the combined effect of IAB inflation and diastolic recoiling of the aorta, recordings were made with the IABP operating in 1:1 and 1:2 with and without the artificial heart. When the balloon was simply pumping against standstill conditions, the IABP was driven by a patient simulator (System 90 Series IABP Trainer, Datascope) which was set at a heart rate of 60 bpm. Steady-state intra-aortic pressure was 66 mm Hg, to simulate mean diastolic pressure in patients.

Multiple beats were analyzed for each condition. Figure 2 shows typical examples of P_{tip} and Q_{tip} recordings during 1:2 assistance, without (top) and with the artificial heart (bottom) for a control and its following assisted beat.

The coronary, subclavian and carotid Q measurements and Q_{tip} were integrated with respect to time as shown in Figure 2 (for Q_{tip}), in order to derive the blood volume (V) displaced through the respective branches and upstream the IAB tip, due to inflation. By subtracting V_{tip} from the nominal balloon volume we derived an approximation of the volume displaced downstream. The volume displaced upstream from the IAB tip, V_{tip} , without going through the coronary or the arch branches is stored in the compliant aortic wall and is referred to as $V_{compliance}$.

Statistical analysis

Data are expressed as mean \pm SD. Statistical significance was assumed at $P < 0.05$.

For the *in vivo* data, results between assistance frequencies 1:1, 1:2 and pump off were compared with ANOVA with repeated measures, followed by contrast analysis (SPSS v 15.0, IL, USA). Due to the small patient population, a more elaborate statistical analysis taking into account possible interactions from factors such as balloon size, could not be performed.

For the *in vitro* data, statistical comparisons were only made with and without the artificial heart, for each balloon size and assistance frequency, with unpaired t-tests. Comparisons between the assistance frequencies or the balloon sizes were not considered to be of important clinical information and were not performed.

Results

***In vivo* results**

Hemodynamic signals

Diastolic aortic pressure augmentation during inflation was demonstrated by a steep rise in the P_{ao} signal of the assisted beat (Figure 1) and coincided with a negative peak in Q_{ao} , induced by blood volume displacement towards the aortic root. This peak was either overlapping with aortic retrograde flow (Figure 1A), or followed immediately after, as a distinct second negative peak (Figure 1B).

Volume displacement

During 1:1 assistance, V_{root} was $6.4 \pm 4.8\%$ of the IAB volume and increased to $10.0 \pm 5.0\%$ during 1:2, but the difference between the two assistance frequencies was not statistically significant ($P = 0.16$).

Hemodynamic parameters

With 1:1 assistance, mean aortic pressure increased by 11.2% (61.6 ± 16.5 vs 68.5 ± 16.4 mm Hg, $P < 0.005$). The increase was 20.2% with 1:2 assistance (58.8 ± 17.1 vs 70.7 ± 17.9 mm Hg, $P < 0.0001$) and it was significantly higher with respect to 1:1 ($P < 0.05$). Mean systolic LV pressure significantly decreased during 1:1 assistance by 8.7% (76.6 ± 21.0 vs 69.9 ± 19.8 mm Hg, $P < 0.0005$) and similarly during 1:2 there was a decrease of 4.6% (73.8 ± 22.6 vs 70.4 ± 20.7 mm Hg, $P < 0.05$). Mean aortic flow increased significantly during 1:1 by 26.4% (2.92 ± 1.06 vs 3.69 ± 1.29 l/min, $P < 0.01$) and by 13.0% (2.99 ± 1.27 vs 3.38 ± 1.25 l/min, $P < 0.05$) during 1:2.

In vitro results

Hemodynamic signals

Early-diastolic pressure augmentation was evident in the P_{tip} recording (Figure 2B) during IAB inflation, similarly to Figure 1. The same finding can also be observed in Figure 2A, but with no heart function. Both with and without the artificial heart, inflation was accompanied by a peak in Q_{tip} which was caused by fluid volume displacement towards the aortic root.

Volume displacement

Figure 3 illustrates the percent distribution of IAB-induced flow during inflation in the coronaries, carotids, subclavians, compliant aortic wall and downstream the balloon, without (top) and with (bottom) heart function simulated by the artificial heart. The results correspond to a 25 cc IAB at assistance frequency 1:2. Overall, when the balloon was counterpulsating with the artificial heart, less

fluid volume was stored in the compliant aortic wall (5.3 ml vs 11.1 ml) and more was displaced downstream the balloon (10.4 ml vs 7.9 ml) and overall through the arch and coronary branches (9.3 ml vs 6.0 ml). The volume displaced through both left and right coronary branches was 1.0 ml without and 0.9 ml with the artificial heart.

Figure 4 presents the volume distribution in ml for a 40 cc balloon during 1:1 IABP support without and with heart function simulation. Similarly to the findings illustrated in Figure 3, with the artificial heart less fluid volume was stored in the compliant aortic wall (14.0 ml vs 21.8 ml) and more was displaced downstream the balloon (13.8 ml vs 9.8 ml) and through the arch and coronary branches (12.2 ml vs 8.4 ml). The total volume displaced through the coronary branches was 1.8 ml as opposed to 1.5 ml without the artificial heart.

Qualitatively, these findings remained consistent between different balloon sizes and different assistance frequencies (Table 1).

Discussion

This study shows that the blood volume displaced *in vivo* towards the coronary circulation during IAB inflation is no more than 10% of the nominal balloon volume. These results are in agreement with our *in vitro* data, which demonstrate that the fluid volume that passes through the coronary branches during inflation is less than 5% of the IAB volume. The *in vitro* investigation further revealed that a large percentage of the fluid volume displaced upstream the IAB tip during inflation is stored in the compliant aortic wall. This percentage was almost two times higher when the artificial heart was not used for simulating the native heart function.

Augmentation of coronary perfusion during inflation

Both the *in vivo* and *in vitro* results show that V_{root} and V_{cor} , respectively, are only a small fraction of the total balloon volume, with the rest of V_{tip} being distributed between the arch branches and stored in the compliant aortic wall. In humans V_{root} was 6.4% during 1:1 and 10.0 % with 1:2 IABP support. *In vitro* and with the artificial heart simulating heart function V_{cor} was even smaller, 3.7% and 3.8%, respectively.

Even though V_{root} *in vivo* and V_{cor} *in vitro* are small, an additional blood volume of 1-2 ml in the coronary circulation is a significant increase to baseline coronary blood flow (CBF). In humans with healthy coronary vessels, mean CBF of 200 ml/min and heart rate of 75 bpm (13), provide approximately 2.5 ml of blood to perfuse the coronary circulation during each heart cycle. Therefore an augmentation of 1-2 ml due to the IABP represents a significant increase in CBF.

The increase of coronary flow *in vitro* in the experiment without the artificial heart simulated the clinical setting during cardiopulmonary bypass and aortic clamping. The results suggest that IABP assistance also may have a role to play in CABG patients to improve coronary perfusion in the immediate postoperative period, when the heart is stunned after cardioplegia, CPB and the consequent inflammatory cascade.

Augmentation of coronary perfusion during IABP support has been quantified in a microsphere study in sheep (11). The authors measured myocardial perfusion using microspheres, in myocardial regions supplied by an obstructed artery or by normal vessels in sheep. Measurements were taken at control conditions and during IABP counterpulsation with a 40 cc IAB. In the regions supplied by healthy coronary vessels, CBF was 0.55 ml/min/g at control and 0.65 ml/min/g during counterpulsation. For an average heart weight of 300 g, coronary perfusion would therefore be 2.75 ml at baseline and 3.25 ml with IABP support. Despite the differences in the experimental settings which make a direct quantitative comparison of these results with ours difficult, both studies are in agreement in that the percentage of IAB volume that reaches the coronary circulation is small and in that this small percentage is however a large contribution to baseline coronary perfusion.

Our *in vitro* measurements were obtained in unobstructed branches and it would therefore be rather difficult to extrapolate the above observations to stenotic coronary vessels. In the presence of a stenosis the effect of the IABP on CBF depends on the severity of the stenosis; the more severe the stenosis the smaller the augmentation in coronary perfusion, with the potential of even a reduction in CBF in cases of severe stenoses (7, 14-17).

Upstream IAB volume *in vitro*

V_{tip} has been quantified *in vitro* in a straight latex tube for different IAB sizes and it was approximately 57% of the nominal balloon volume (18). Head pressure was 24 mm Hg and the IAB

was operated from standstill. Considering the different experimental settings, these results are not substantially different from those of the present study, where V_{tip} was 72.6% at 1:1 and 68.1% at 1:2 without the artificial heart, and 63.1% and 62.0%, respectively, with the artificial heart.

Volume storage in the aorta *in vitro*

It was not possible in the *in vitro* experiments to determine the distribution of stored volume along the compliant aortic wall, but, merely due to size, it can be speculated that the larger storage capacity lies in the upper aorta, in the portion upstream from the IAB tip. The length of this segment in the silicone aorta was 17 cm, with an average diameter of 24 mm. Measurements with ultrasonic crystals of the diameter of the upper descending sheep aorta during IAB counterpulsation, showed an increase of 4.4% between systolic diameter and maximum diastolic diameter during inflation (19). An increase of 4.4% in the mean diameter of the 17 cm segment of the silicone aorta can be translated to an increase of 6.5 ml of its total volume capacity during inflation. This volume is not dissimilar to the results of our *in vitro* study, showing volumes of 5.79 ml during 1:1 and of 5.29 ml during 1:2 assistance stored in the compliant aortic wall during the inflation of a 25 cc IAB. The corresponding volumes for a 40 cc IAB are larger, most likely because the aortic model was overstretched during IAB inflation, in a way that would have been prevented *in vivo* by using a smaller IAB size.

Effect of heart function on IAB counterpulsation

When the IAB was counterpulsating with the artificial heart, V_{tip} was smaller than when operating without the artificial heart. However, overall more volume was distributed to the arch and coronary branches and less was stored in the compliant aortic wall. This effect is clearly demonstrated in

Figures 3 and 4 and in Table 1.

Since in both *in vitro* setups there is minimal diastolic or no flow in the aorta during IAB inflation, this difference in volume distribution can be associated with a difference in compliance (4). When IAB inflation follows a cardiac systole, due to the Windkessel effect taking place in the aorta during diastole, the elastic aortic wall will be recoiling at the same time the inflating balloon is trying to expand it. Due to these opposing actions, aortic compliance is lower and the fluid volume that can be stored in the aortic wall is less than the volume that can be stored when the aorta can freely expand during inflation. The fluid volume not stored in the compliant aortic wall in the presence of heart

function is then distributed elsewhere (Figures 3 and 4). The discharging of the fluid volume stored in the compliant aortic wall is demonstrated in Figure 2A, by the exponential rise in P_{tip} between 15.5 and 16.5 s.

This result underlies in an indirect way the importance of arterial compliance on IABP performance. These findings are in agreement with previous studies stating that the efficiency of the IAB is limited in highly compliant aortas (20-22).

Effect of assistance frequency *in vivo*

The blood volume displaced towards the coronary circulation during the assisted beat of the 1:2 support is less than the combined volume displaced by two consecutive beats during 1:1 support. Although the results are not statistically significantly different for this patient population, it is possible that in a larger population differences would be more pronounced.

Methodological considerations and limitations

It is expected that the reduction in systolic P_{LV} during 1:1 assistance in patients will induce coronary vasoconstriction due to the reduced myocardial oxygen demand (23) and therefore reduce CBF, while on the other hand volume displacement due to inflation simultaneously tends to increase it. This mechanism could not be duplicated *in vitro*, and it is difficult to predict how this practically affected V_{cor} . Other *in vivo* pathological indications for using IABP such as cardiogenic shock and unstable refractory angina could not be simulated as their mechanism involve sympathetic and parasympathetic nervous activities that couldn't be replicated *in vitro*.

Conclusions

The blood volume displaced towards the coronary circulation due to IAB inflation is only a small percentage of the nominal IAB volume. However small compared to the IAB volume this percentage might be, it is still a significant percentage of baseline coronary perfusion.

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Tables

Table 1: Mean volume distribution for the 25 and the 40 cc balloons.

V (ml)	Balloon 25 cc				Balloon 40 cc			
	1:1		1:2A		1:1		1:2A	
	noHeart	Heart	noHeart	Heart	noHeart	Heart	noHeart	Heart
R subclavian	1.09 ± 0.10 [*]	0.98 ± 0.08	1.02 ± 0.15	1.05 ± 0.17	1.70 ± 0.15	1.62 ± 0.32	1.49 ± 0.16 [*]	2.03 ± 0.31
L subclavian	1.21 ± 0.12 [*]	0.95 ± 0.19	1.12 ± 0.11 [*]	0.83 ± 0.13	1.79 ± 0.14	1.87 ± 0.39	1.65 ± 0.21	1.57 ± 0.27
R carotid	0.96 ± 0.03 [*]	3.45 ± 0.06	1.35 ± 0.03 [*]	3.54 ± 0.08	1.54 ± 0.05 [*]	4.13 ± 0.04	1.94 ± 0.12 [*]	4.59 ± 0.06
L carotid	1.00 ± 0.03 [*]	3.04 ± 0.14	1.55 ± 0.03 [*]	2.98 ± 0.03	1.61 ± 0.05 [*]	3.15 ± 0.08	2.11 ± 0.04 [*]	3.37 ± 0.05
R coronary	0.47 ± 0.01	0.48 ± 0.01	0.43 ± 0.01	0.50 ± 0.01	0.90 ± 0.01	0.82 ± 0.01	0.75 ± 0.01	0.85 ± 0.01
L coronary	0.58 ± 0.00 [*]	0.44 ± 0.01	0.56 ± 0.01 [*]	0.44 ± 0.01	0.87 ± 0.02 [*]	0.65 ± 0.01	0.74 ± 0.05 [*]	0.66 ± 0.01
upstream	17.39 ± 0.92 [*]	15.13 ± 0.89	17.14 ± 1.10 [*]	14.61 ± 0.20	30.22 ± 2.18 [*]	26.25 ± 0.90	27.10 ± 1.45	26.18 ± 0.89

Volume (V, in ml) displaced into the arch and coronary branches and upstream the IAB tip *in vitro* due to IAB inflation at different assistance frequencies, without ('noHeart') and with the artificial heart ('Heart'). R, right; L, left. Mean values for the subclavians and the aorta are based on 16 measurements, while for the other branches 8 measurements were available. ^{*} $P < 0.005$, comparing 'noHeart' to 'Heart'.

Figure Legends

Figure 1: Hemodynamic waveforms *in vivo* during 1:2 IABP support for a control (top) and an assisted beat (bottom) in two different patients (A and B). P_{ao} , aortic pressure (solid black); Q_{ao} , aortic flow (filled grey). In cases of correctly-timed inflation, like the one illustrated in A, V_{root} was derived by subtracting the intrinsic backflow of the control beat from the backflow of the assisted beat (both areas shaded in dark grey). In cases of late inflation, like the one in B, V_{root} was derived directly from the assisted beat, by integrating the area shaded in dark grey.

Figure 2: Pressure (P_{tip} , solid black) and flow (Q_{tip} , filled grey) *in vitro* during 1:2 IABP assistance. Arrows indicate the onset of inflation and deflation. No artificial heart was connected to the system in A, while the IABP was synchronized to the artificial heart in B. V_{tip} was derived by integrating the area shaded in dark grey in each case.

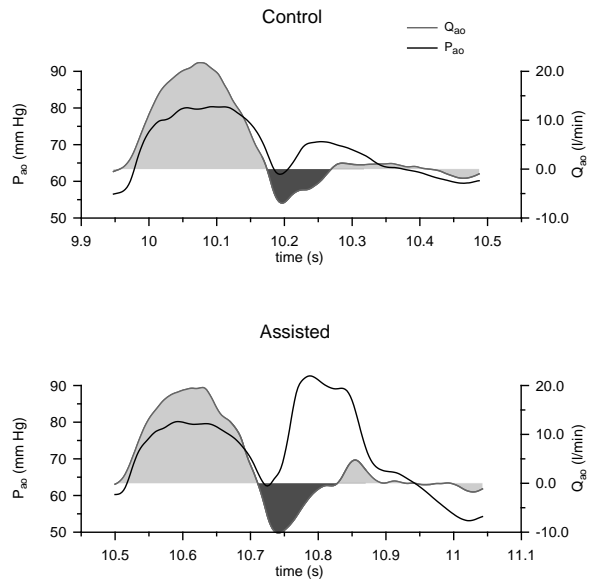
Figure 3: Percent distribution of the total volume displaced upstream and downstream a 25 cc IAB during inflation at 1:2 assistance, (A) without and (B) with the artificial heart connected to the *in vitro* set up. L, left; R, right.

Figure 4: Schematic diagram of the upper portion of the artificial aorta, showing the tip of the IAB and the approximate locations where flow was measured in the coronary and arch branches. The fluid volume that passed through each branch *in vitro* due to the inflation of the 40 cc IAB at 1:1 frequency, is noted both for the case of no artificial heart connected to the system and with the artificial heart. L, left; R, right.

Figures

Figure 1

A



B

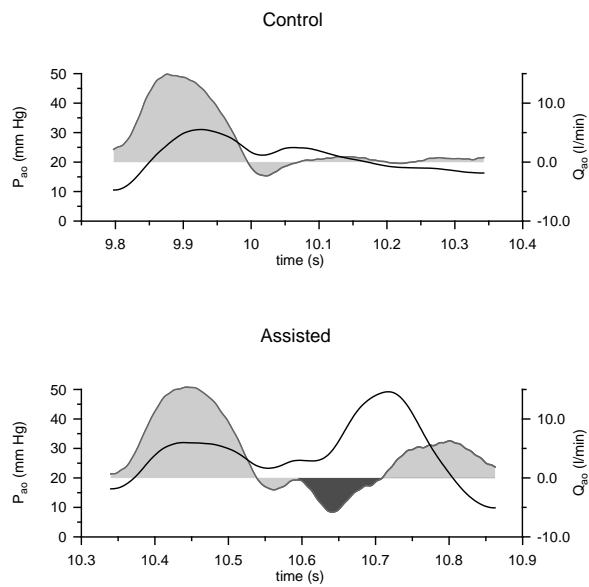
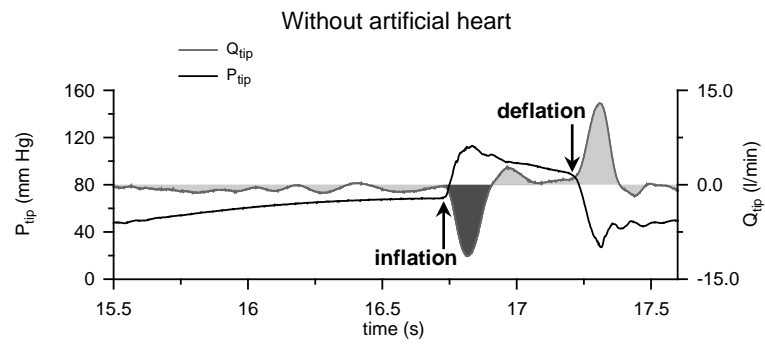


Figure 2

A



B

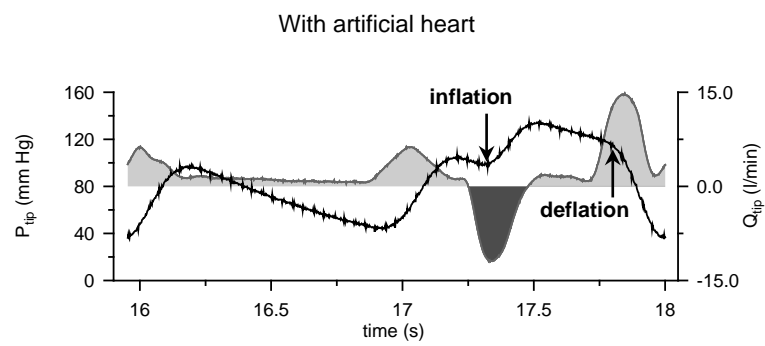
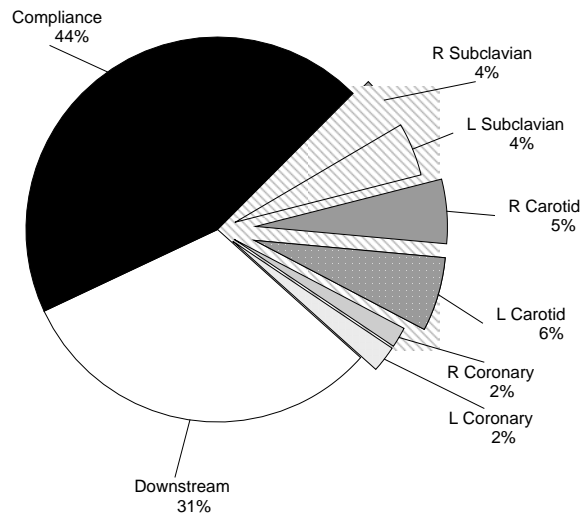


Figure 3

A

without artificial heart
1:2



B

with artificial heart
1:2

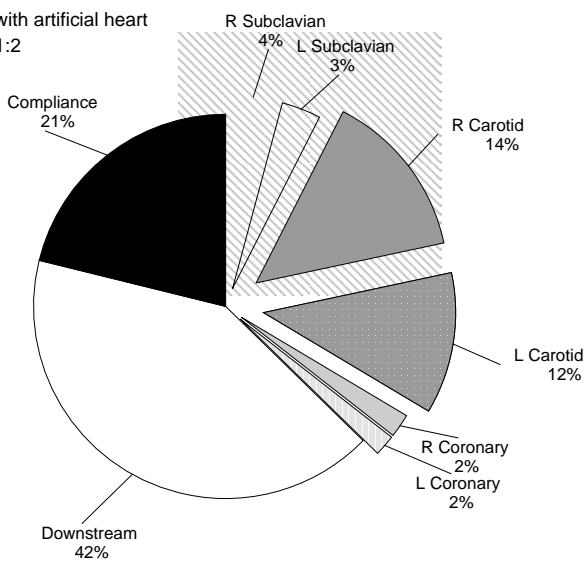


Figure 4

L Coronary
Without: 0.87 ml
With: 0.65 ml

