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Analysis and design of a thrombectomy device by using simulation techniques

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Abstract

Purpose:

In this work, we present the analysis, design and optimization of one experimental device recently developed in the UK, called the 'GP' Thrombus Aspiration Device (GPTAD). This device has been designed to remove blood clots without the need to make contact with the clot itself thereby potentially reducing the risk of problems such as downstream embolisation.

Method:

To obtain the minimum pressure necessary to extract the clot and to optimize the device, we have simulated the performance of the GPTAD analysing the resistances, compliances and inertances effects. We model a range of diameters for the GPTAD considering different forces of adhesion of the blood clot to the artery wall, and different lengths of blood clot. In each case we determine the optimum pressure required to extract the blood clot from the artery using the GPTAD, which is attached at its proximal end to a suction pump.

Result:

We then compare the results of our mathematical modelling to measurements made in laboratory using plastic tube models of arteries of comparable diameter. We use abattoir porcine blood clots that are extracted using the GPTAD. The suction pressures required for such clot extraction in the plastic tube models compare favourably with those predicted by the mathematical modelling.

Discussion & Conclusion:

We conclude therefore that the mathematical modelling is a useful technique in predicting the performance of the GPTAD and may potentially be used in optimising the design of the device.

1 Introduction

Stroke is one of the major causes of mortality in the world-wide. More than 120,000 strokes per year occur in the UK [1]. Six per cent of National Health Service and Social Services expenditure is spent on stroke management.

Thrombosis is produced by the formation of a clot inside blood vessels causing an abrupt interruption of the blood flow [2]. In the cerebral arteries, this occlusion can result from the migration of a clot that has formed at another location. The process concerning the removal of this obstruction involves catheterisation [3].

Although thrombolytic agents such as Alteplase are used to dissolve such, there are limitations on their use. Consequently, alternative methods of treatment have been developed which includes Thrombectomy Devices. A number of Thrombectomy devices using a variety of methods have now been developed to facilitate clot removal. We present research involving one such experimental device recently developed in the UK, called a 'GP' Thrombus-Aspiration-Device (GPTAD) [4]. This device has the potential to bring about the extraction of a thrombus. Although the device is at a relatively early stage of development, the results look encouraging.

The main objective of the work we present is to obtain the minimum pressure required to perform blood clot extraction and to check that this pressure as well as the time required to complete the clot extraction are reasonable for possible potential use on a patient and are similar to experimentally obtained data. In addition, we ascertain if the cerebral arteries are able to support the suction force to which they are subjected. We also determine that the components comprising the proposed device, based on the 'GPTAD' probe, and the blood flow generate speeds that fall within admissible parameters. We believe that such studies may help in optimising the design of the GPTAD and its possible future use in patients with thrombosis.

This paper gives a brief description of the proposed device, based on the 'GPTAD' device, as well as the parts comprising it. The model used for the simulation is

described as well as the phenomena considered, and, in addition, the values of the parameters used are defined. Finally the results obtained and the conclusions of this study are described.

2 'GP' Thrombectomy Device

A schematic view of the GPTAD is shown in figure 1. It has potential advantages in clot removal procedures in that it does not need to touch the clot to facilitate clot removal (therefore there is less risk of downstream embolisation), and it has no moving parts (therefore less risk of breaking). In vitro testing of the GPTAD to remove abattoir porcine blood clots in plastic tube models of arteries and modelling has been undertaken [5][6][7].

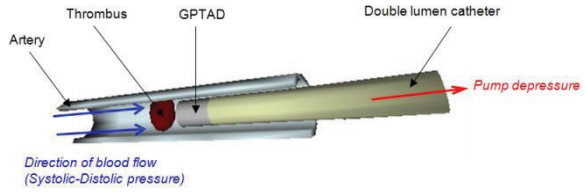

Fig. 1 Schematic diagram of the clot removal device.

The GPTAD device assembly involves using a vacuum pump (that provides the suction pressure for removal of the clot), joined to a very long double lumen catheter (~100 cm long and ~2.0-5.0 mm in diameter); the 'GP' device is located at the end of this catheter (same diameter and a length of 20 mm). This GPTAD is introduced into the carotid artery via a transfemoral approach to the lower limb such that the GPTAD is positioned in close proximity to the occluding blood clot, at a distance of approximately 3 mm from it. Then the suction pressure is slowly increased until clot capture occurs and the clot is extracted. The clot crosses the 3 mm "gap" (filled with blood) that separates it from the GPTAD and when clot capture occurs the entire device is then removed from the body.

It is currently being developed as a potential thrombus aspiration device through a series of in-vitro studies. This device has the potential to be used in relatively small arteries too. It has no moving parts and therefore should reduce the risk of breakage in a vessel. Since it does not touch the clot itself it should also reduce the risk of clot disruption and downstream embolisation. Thrombectomy is achieved by aspiration through a catheter in which the 'GPTAD' device is embedded. The internal surface has been mathematically optimized. It is also potentially associated with low forces at the periphery of the device which may therefore reduce the risk of arterial collapse during aspiration of the clot [8].

3 In-Vitro Experimental Considerations

Clearly removal of arterial thrombus depends on several factors including the size of the clot, its location, and the force of attachment of the clot to the vessel wall. In designing any arterial clot removal device, many factors must be taken into account e.g. mechanical and biocompatibility factors relating to the biological tissue, also material strength and flexibility of the device. The risk of damaging or penetrating the vessel wall must also be considered, together with potential clot dislodgment then causing further distal damage. Taking into account these requirements, the blood clot removal device has been modelled using Bond graph modelling techniques.

The design of the final device was the result of a series of modifications made from the original design, testing their efficacy in terms of their potential to remove jelly like clots. The main parameters measured each time were the time taken to remove the clot and the vacuum pressures required to remove the clots.

Considering a simple case where a clot is located at one specific point on the vessel wall, it has been previously studied by Fung [9]. In this study, the occlusion of the artery is defined by the angle that the clot subtends in relation to the circumference of the artery. Rekhter [10] considered the effect of clots associated with atheromatous plaques and found values for the typical force with which an atheromatous plaque is attached to an artery wall. Dr. CJ Flannery [11] determined that a thrombus can be detached at a maximum upstream pressure of ~450 mmHg, which is six-tenths of an atmosphere, or roughly 4 times mean arterial blood pressure. The total thrombus detachment strength was calculated to be approximately 8.9 mN, i.e. thrombus removal from a stenosis was measured with a force of detachment being at the high end of about 9 mN. In all analysed cases by Dr. Flannery, thrombus adhesion strength was between 0.25 and 9 mN. This is consistent with the below in vitro measurements of glycoprotein surface density and adhesion strength found in literature review. From the previous values, in our work we will use 10 mN.

In vitro experiments were also undertaken to measure the forces (in kPa) required to remove the jelly, using the apparatus described in figure 2 below [12]. A vertical tube supplied with tap water at the lower inlet to create a water column is placed with its length of 0.5 metres to be accessed by the tap and the suction line. During suctioning the water level is kept constant by re-supplying water in the same amount as the suctioned volume. The required suction pressure at the suction line is supplied via a vacuum source. The vacuum source is an evacuated glass vessel (1 L) connected to a vacuum pump. Suction starts by opening a valve (clamp) in the suction line when the device is in place. In the shown case, an artificial clot was used to simulate the blood clot because it has similar mechanical properties and was readily available.

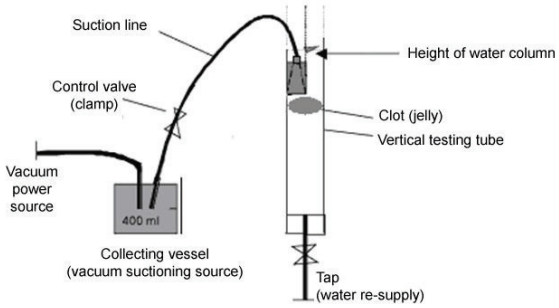

Fig. 2 Apparatus used in the experiment.

From the previous experiments, it was found that the force required to remove a jelly-like clot a few mm in diameter using a GP clot removal device (of internal diameter 3mm and external diameter 4mm and length 10mm) was 10Kpa. The removal time for this jelly like clot was 15 seconds and the volume of fluid extracted in the process was 17 ml. These results (typically 15kPa) are in good agreement with the results obtained in the practical experiments quoted above (10kPa).

4 Modelling the GPTAD Device

The main objective of this study is to introduce a model that can be used investigate and assist in the final design of the GPTAD. In this work we investigate the potential performance of the GPTAD device under different conditions of blood flow, size of blood clot, in a given vessel.

The method chosen for the representation and simulation of the GPTAD in this instance is the Bond Graph technique [13-14-15], which allows assimilating the model to an electric circuit made up of inductances, capacitances and resistances. Therefore, it is possible to obtain the results in a simple way by evaluating flows and efforts that join and connect the components of the model. To obtain the simulation of the model, Bondin © software will be used [16]. This program allows us to obtaining the evolution of the characteristic parameters of the model as well as letting them be compared.

To generate the correct model, it was necessary to analyze the inertances due to mass of fluid, the compressibility that the blood and artery are subjected to, and finally the resistances that appear when fluid and blood clot flow into the catheter [17].

First the pump, which is the component that creates the necessary pressure to carry out the extraction, is positioned. It can be represented by a variable pressure source (Se) whose value will increase from zero to a non-determined value suitable for carrying out this operation and will be obtained from the optimization of the developed model. The time taken to reach the maximum value of pressure has been obtained from experience and must be about 3 sec., after which time the pressure provided by the pump remains constant.

The pump links to the catheter, a 110 cm long 1 mm diameter hollow cylindrical tube which is joined to the 'GPTAD' device of the same diameter and of length 20 mm. In order to represent both elements, they are considered as several pipe sections bearing in mind the different phenomena that take place in their interior: load and inertia loss, and fluid compressibility [17].

Firstly, the flow inertia to be overcome in its movement is taken into account and considering a section with circular geometry it must be represented by a type 'I' port and a type '1' junction and can be modelled with this expression:

$$\square = \frac{\rho \cdot \square}{\pi \cdot \left(\square/2\right)^2} \qquad (1)$$

where 'ρ' is the blood density, 'L' the length of the pipe section and 'D' its diameter.

The blood has been deemed to be an incompressible fluid and this eliminates the blood compressibility effect; if we wanted to take it into account, it should be included as a compliance that produces a decrease in volume when the pressure required for compression is increased. This behaviour would be dependent on the Bulk coefficient for blood, 'B' and it could be defined as a capacitance of value 'K'.

Due to the friction between the liquid particles and the pipe walls, load losses appear. Since we are dealing with straight pipes in our model, only linear load losses are taken into account. As the pipe is horizontal and of constant cross section in each section, the load loss is reduced, since there is a pressure loss as the fluid advances along the pipe, the loss being progressive and proportional to the length of the pipe. This pressure loss can be represented by a resistance and a type '1' junction. If we assume that when artery is 100% occluded there is no flow, and since the Reynolds number is only significant if turbulent flow is involved, the equation that governs its behaviour can be determined by following expression (2), where 'η' is the dynamic viscosity of the blood flow, 'L' the length of the pipe section and 'D' its diameter.

$$\square = \frac{128 \cdot \eta \cdot \square}{\pi \cdot \square^4} \qquad (2)$$

The flow of blood may well be turbulent at an arterial bifurcation for example, or in the case of an atheromatous plaque associated with a pathological blood clot, not existent in this case. In these situations it would be necessary to determine the load losses for turbulent flow and taking into account Reynolds number.

Following on from the tube corresponding with the catheter, the 'GPTAD' device (see figure 1) must be positioned such that it can be represented with its corresponding values.

Due to the artery being located at the end of the 'GPTAD' device, it is necessary to consider the transition between both elements as a secondary load loss caused by the difference in diameter of the 'GPTAD' probe and the artery respectively and the subsequent variations in flow (deflecting nozzle in figure 4). These load losses can be represented as a resistance and can be calculated with the following expression (3), where 'ρ' is the blood density, 'Q' is the flow which circulates in the section between the end of the 'GPTAD' probe and the artery, and the diameter 'D' is the mean value between the probe (D_{GP}) and the artery (D_{artery}).

$$\square = 8 \cdot \rho \cdot \xi \cdot \frac{\square}{\pi^2 \cdot \square^4} \qquad (3)$$

The load loss coefficient 'ξ' is a dimensionless parameter that quantifies the loss produced and depends on the geometry of the conical aperture.

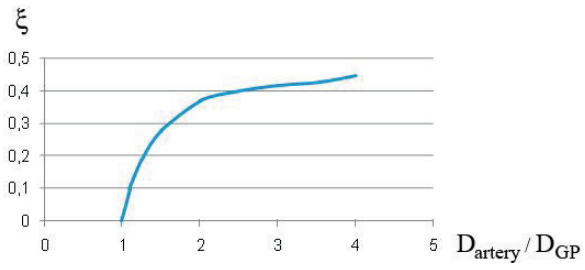

Fig. 3 Load loos coefficient values.

Considering the results obtained in figure 3, the ideal value for the design of the 'GP' diameter is that which corresponds with the same diameter that the artery, in which case it would create zero load loss. In patients it is not possible to use the exact value and considering it to be a narrowing with $D_{GP} = 1.5 \cdot D_{artery}$, this value can be considered as being 0.3 in the best case.

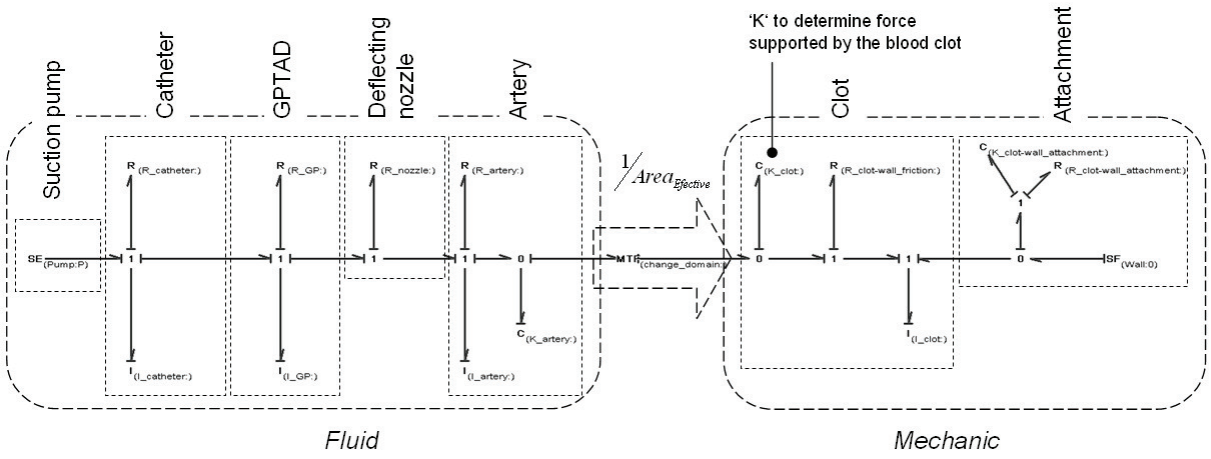

Fig. 4 Full model of the GPTAD

The artery can be included in the model as another section of a pipe, similar to the catheter and the 'GPTAD' device and it must be defined by the loss of linear load 'R' and the inertia 'I' (figure 4). In addition, it is necessary to insert a parameter that represents the compressibility of the artery, in line with its Young's modulus:

$$\square = \frac{\square \cdot \square}{\square_0 \cdot 2 \cdot \square_0} \qquad (5)$$

where 'E' is its Young's modulus, 'h' is the thickness of the artery, 'V_0' is the artery initial volume and 'r_0' is the artery initial radius. According to Guthold et al. [18], fibrin fibres in the clot deform elastically, not plastically, and the Young's modulus of fibrin is about 1 MPa.

Once the elements corresponding to pump, catheter, 'GPTAD' device and artery have been defined by fluid mechanics, it is necessary to change from the domain of hydraulics to mechanics, to be able to evaluate the movements and efforts in clot removal, as well as to define the physical friction between the clot and the artery. This domain change is carried out by a Transformer (TF) element. To calculate the value of the coefficient defining this element, the change in the definition of the flow before and after this element is evaluated; it is known that there is no leakage around the clot and no blood gets past the clot when it is causing 100% occlusion of an artery. The coefficient must be determined by evaluating the required change between both domains; before the TF element, the flow is in the hydraulics domain, while afterwards, it is in the mechanical domain. Then, the coefficient of the TF element must be the inverse of the section of artery.

Whilst in the mechanical domain, in the model it is necessary to insert a compliance between the end of the artery and the beginning of the clot to obtain the force supported by the clot each moment; this force is necessary to begin or stop the movement of the blood clot in accordance with the minimum necessary pressures obtained in section 3.

The friction between the clot and the arterial wall creates a resistance factor. The value of this parameter must be variable depending on whether the clot has begun its movement (dynamic friction) (3rd case in figure 5) or before it has begun to move (static friction) (1st and 2nd cases in figure 5) during the clot extraction procedure.

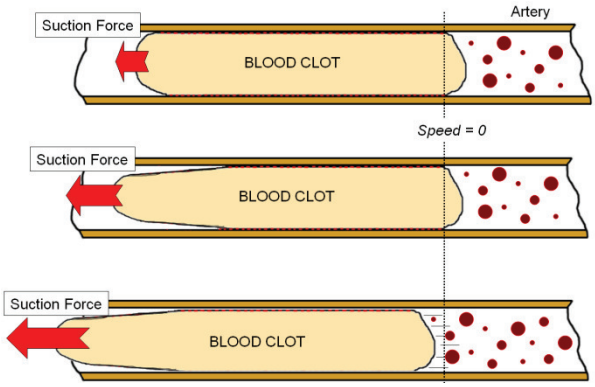

Fig. 5 Influence of the suction force over blood clot

When the clot begins to move the friction decreases considerably. This value is obtained from the Stokes equation and can be given a value of $2.5 \cdot 10^{-6}$ N·s/m for the static friction and an order of magnitude lower than for the dynamic friction. The transition between both values marks the beginning or end of the clot movement.

In addition to the compliance and the resistance inserted, the model must have an inertance that represents the mass of the clot (~0.05 - 3 gr.) (figure 5).

Finally, to ensure that the clot remains at rest while the force existing at its beginning is less than 10 mN, a compliance-resistance system joined to a wall (zero flow source) must be used (figure 4). In this system, while the clot does not receive the force of minimum suction, it has zero speed. However, when it begins its movement, the compliance-resistance system must be cancelled allowing its extraction.

Therefore, while the force representing the deformation of the clot is lower than 10 mN, it will remain attached to the wall (1st and 2nd cases in figure 5), thereby preventing any movement. To the contrary, if the force exceeds this value, the model will cause the bond imposed by the compliance-resistance system to be eliminated with the clot becoming free and moving in accordance with the suction pressure acting on it from the system, thus allowing it to be removed (3rd case in fig. 5).

5 Results

The aim of this simulation is to compare the extraction of a clot in different arteries (5.5 mm, 3.2mm and 2.5 mm) considering different clot lengths (0.5 cm up to 5.0 cm each case) and 100% occlusion; in our case, 90% will be blood clot and 10% atheromatous plaque. An arterial occlusion of 90% will modify the area in which the suction force acts, considering that the clot reduces the cross-sectional area of the artery.

The use of arteries of different diameters will influence directly the diameters of GP device that can be used in a given artery and hence those used in our modelling presented here. In the previously arterial diameters, the standard elements ('GP' and catheter) would have normalized values; it being necessary to choose the nearest diameter value to be inserted into the artery (5.0 mm, 3 mm and 2.0 mm respectively).

The existence of different clot lengths will affect the mass of the clot being removed (0.06 gr. up to 3 gr.), and increase the time taken for clot removal as the value of the clot length increases.

The following figures show the time taken to create the necessary suction force to move the clot across the 3 mm between the clot and 'GP' device, for different pump suction pressures, diameters and clot lengths.

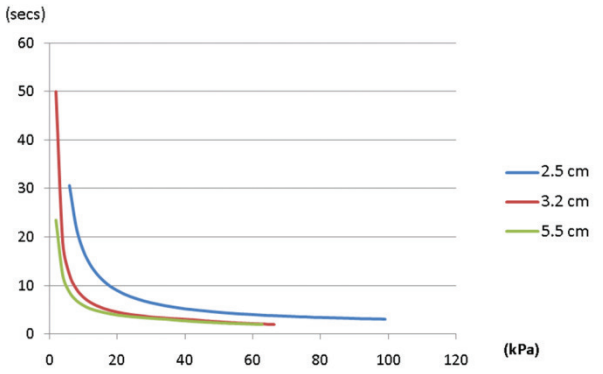

Fig. 6 Pressure (kPa) vs time (secs)

The previous figure indicates the time needed to move the clot across the 3mm gap filled with blood, to enable clot capture to occur for the case of a blood clot length 5cm in length. We observe that there is a difference on applying vacuum suction in each artery. The time taken to remove the blood clot in each instance is also different for each case.

There are clearly differences in the times taken to remove the blood clot of various different diameters. While for a pressure of -30 Kpa the required time is below 7 seconds in all cases, the use of smaller suction pressures causes the range of times for clot removal to increase near to 1 minute in some cases, e.g. with -4kPa pressure. In some instances, lower pressure sometimes increases the required time to more than 10 minutes – these cases correspond with the smaller arteries. It should be noted that the pressure losses are inversely related to the artery cross-section. It is possible to speculate that a minimum required suction pump pressure must be around -4 kPa or -6 kPa, and that the corresponding clot removal times would then take less than ¾ or ½ minute.

In figure 7 results are shown for the different diameter arteries and with a -6 kPa pressure pump, for each length of clot, together with the time when the clot begins to move until and it reaches the end of the 'GP' device. In considering the results of the modelling presented in figure 7, it can be seen that clots with a length between 1 cm to 2 cm, need relatively short times for clot capture (2-12 secs.). However, clots with a size between 4 cm to 5 cm show a bigger variation in the time involved with different diameters (12 secs up to 30 secs).

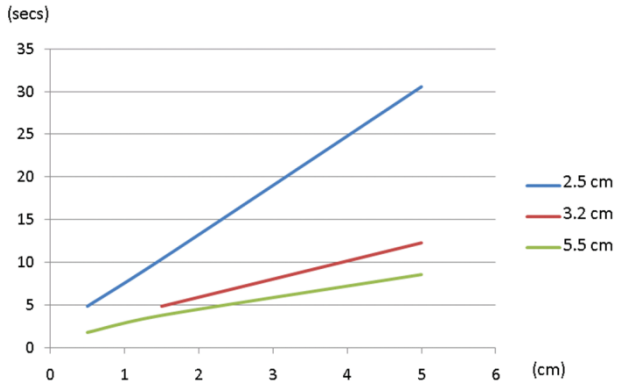

Fig. 7 Length clots (cm) vs time (secs)

Higher clot removal times result when the clot lengths are greater e.g. with a 5 cm clot length in the smallest arteries.

These results indicate the importance of carrying out clot extraction as quickly as possible, and indicate the potential uses and importance of such modelling.

6 Conclusions

Analyzing the obtained results, they are coherent with the physic laws and, in addition, they are very similar to in-vitro experimentally obtained results by using the same values for each parameter. Actually, only few in-vitro experiments has been done taking into account porcine blood clots and the entire validation of the mathematical model should be done comparing new situations and experiments. After it, the developed model could be used correctly to optimise the final design of the device in terms of materials, roughness or diameters of catheter and GP.

Nevertheless, the development of this simulation model enables us to obtain an estimate of the minimum pressure required to perform the extraction of blood clots of different sizes and for different diameters of arteries. In all cases we have taken the same age for the clot residing in the artery and the same values for the force of adhesion.

This modelling has shown that the suction pressure together with the time required to complete clot removal are reasonable, and should be within acceptable clinical boundaries for any eventual potential use of the GPTAD device in patients. A similar analysis [19-20-21] undertaken for its use in the MCA or the Popliteal artery enables further comparisons to be made. We compare the results of simulation modelling to measurements made in laboratory plastic tube models of arteries of comparable diameter where the GPTAD was applied to successfully extract abattoir porcine blood clots. The suction pressures required for such clot extraction in these plastic tube models compare favourably with those predicted by the simulation modeling. Taking into account the comments done at the beginning of this section, the mathematical modelling presented may potentially be useful in predicting the performance of the GPTAD and could possibly be used in optimising the design of the device.

7 Future Works

The presented mathematical modelling is now being implemented to model and simulate different adhesion forces and a range of percentage arterial occlusions. In this future modeling include the systolic/diastolic pressure effects for case of arterial occlusion below 100% (including clot and plaque).

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