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Original Article

Mechanism underlying the prevention of aneurismal rupture by coil embolization

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(Object) Endovascular treatment with Guglielmi detachable coil has been developed as a less invasive treatment for cerebral aneurysm. The aim of this study is to clarify the mechanism of the preventive effect of coil embolization .

(Method) Two aneurysm models were employed. One was a T-shaped bifurcation tube with a spherical dome made of glass, which was used for the measurement of pressure and visualization of flow pattern. The other model was a T-shaped glass tube with a spherical elastic silicone dome, which was used for the measurement of aneurismal wall displacement due to pulsation of flow.

(Result) 1, Guglielmi detachable coil caused no change in intra-aneurismal fluid pressure. 2, Coil insertion obstructed and slowed intra-aneurismal flow. This flow stagnation in the aneurysm might promote thrombus formation. 3, With increase in numbers of coils anchored at the intra-aneurismal wall, the displacement of the wall was considerably depressed. This suggests that coil insertion decreases the stress on the aneurismal wall.

(Conclusion) 1, Coil insertion depresses the pulsatile aneurysm wall movement, and diminishes the stress of the aneurysm wall. 2, Coil insertion obstructs intra-aneurismal flow and facilitates thrombus formation in the aneurysm. These two factors may operate synergistically to prevent aneurysm rupture.

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1. Introduction / Objective

Pioneered by Guglielmi in 1991[1], endovascular treatment with detachable coils has been developed as a less invasive treatment for cerebral aneurysm[2,3]. Vinuela,et.al demonstrated the safety of the Guglielmi Detachable Coil (GDC) system for the treatment of ruptured intracranial aneuysms[4].

The mechanism by which coil embolization prevents the intra-cranial aneurysm rupture is thought to be the thrombus formation around coils that are inserted to occlude the aneurysm[5].

But several studies have demonstrated the preventive effect of coils on aneurysm rupture in the acute phase, when a thrombus is less likely to have been formed[6,7].Thus the mechanism is still not well understood. In order to elucidate the mechanism of coil treatment, we prepared an experimental model to characterize the dynamics of inserted coils by determining how intra-aneurysm blood flow and pressure are affected.

The aim of this study is to clarify the mechanism of the preventive effect of coil embolization on intra-cranial aneurysm rupture.

2. Materials and Methods

2-1. Experimental apparatus

The schematic diagram of the experimental apparatus used in this study is shown in Fig. 1 (A). Pulsatile flow was produced using a bellows pump and an air tank. The pump rotation and stroke volume were controlled. The pressure profile was adjustable through the air tank. Aqueous glycerin solution was used as the test fluid, the viscosity of which was similar to that of blood. The temperature of the fluid was kept around 36.5°C throughout the measurement.

Two aneurysm models were employed in this experiment. One was a T-shaped bifurcation tube (vessel model) with a spherical dome made of glass. A small hole about 1mm in diameter was opened 6 cm upstream from the bifurcation point and at 3 points on the aneurysm dome, as shown in Fig. 1 (B). This glass model was used for the measurment of pressure and visualization of flow patterns. The other model was a T-shaped glass tube with a spherical elastic dome made of silicone(the thickness of the silicone wall was 150 μm). This model was used for the measurement of aneurysm wall motion due to pulsation of flow.

The diameters of the T-bifurcation models were greater than that of the human artery in the base of the brain. Fluid mechanics states that when the mechanical properties derived from a model experiment are compared with in vivo circulation, the Reynolds number in the model system should be the same as that in the real arteries[8]. In the arteries consisting the circle of Willis, which is the preferential sites for aneurysm formation, the Reynolds number is estimated to be from 300 to 600[9]. The present experiment was thus performed in this Reynolds number range. The pulsation cycle of flow was ranged from 60 to 90/minute. The flow rates of two branched flows were set to be equal throughout the present measurement.

2-2. Pressure measurement and flow visualization

The pressure in the tube and the aneurysm dome was measured with a pressure transducer (Statham P50). The signals from the sensor were amplified, converted from analog to digital data, and then stored in a personal computer. The pressure was measured at three positions of the aneurysm model as described above. A catheter was placed into the aneurysm model from the upstream of the glass vessel to insert coils as the same procedure employed in the clinical treatment. The pressure was measured at each step of coil insertion. After coil insertion, the aneurysm was packed with 9 coils, occupying 22.3% of the aneurysm volume. This amount of coils is considered to be tightly packed (successful packing) in a clinical setting. From such pressure profiles, we can calculate the mean pressure averaged over time (P_{av}), and the difference between maximum and minimum pressures (P_d) in order to evaluate the mechanical effect of inserted coils (Table 1).

The flow patterns around the aneurysm model were

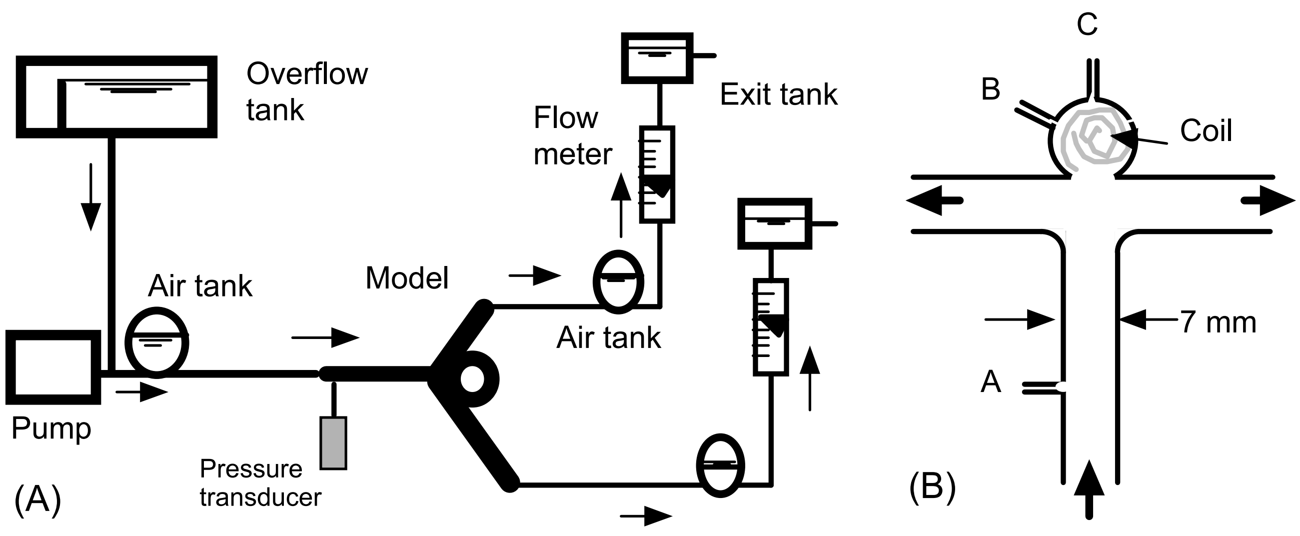

Fig. 1. (A): Schematic diagram of the experimental set-up. (B): Bifurcation aneurysm model. A, B and C indicate the locations of the pressure measurements.

Table 1. Mean pressure Pav and pressure difference Pd measure at three positions in the aneurysm model (Fig.1(B)). Pav: mean pressure averaged over time. Pd: difference between top and bottom of pressure profile. The accuracy of the pressure measurement apparatus is 0.025 mmHg. However, when comparing the values listed in this table, the overall accuracy is limited to 1 mmHg, which is mainly caused by the stability of pumping system in the flow circuit and in part calibration procedure of pressure.

	Pav mmHg			Pd mmHg		
Position	A	B	C	A	B	C
Before	73.78	73.14	73.50	60.81	61.39	61.62
After	73.65	73.00	73.59	60.79	61.42	61.49

Pav: mean pressure averaged over time.
Pd: difference between top and bottom of pressure profile.

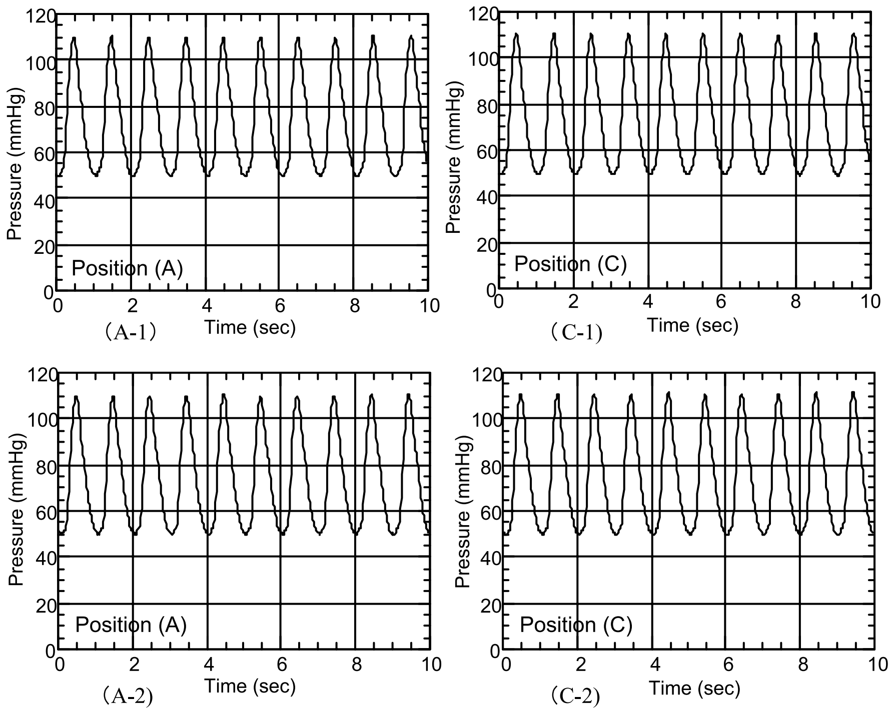

Fig. 2. Pressure profiles measured in the tube (6 cm upstream of the bifurcation point; point A in Fig 1 (B) and at the top of the aneuriysmal dome; point C in Fig. 1(B). Panels (A-1),(C-1): before coil insertion. Panels(A-2),(C-2) after insertion of 9 coils.

visualized with dye and polyethylene micro-particles (approximately 20 to 50 μm in diameter). The flow patterns were recorded with a digital video camera (Canon, MV1), and the video images obtained were processed into frames and captured into an image storage system using a personal computer. These two experiments were repeated several times.

2-3. Measurement of aneurysm wall displacement

Aneurysm wall motion accompanied by pulsatile flow was measured with a laser displacement meter, the resolution of which was 0.2 μm (Keyence, LC-2400). The wall displacement was measured at the top of the aneurysm dome. For each step of coil insertion, the measurement of wall displacement was repeated several times with changing the position of the inserted coils.

3. Experimental results

3-1. Pressure measurement

Typical pressure profiles measured at the model tube and the top of the aneurysm dome are shown in Fig. 2. Panels (A-1)(C-1) and (A-2)(C-2) of Fig. 2 represent the results before and after the coil insertion, respectively.

It could be seen that the pressure profile in the tube (at point A in Fig. 1(B)) was almost the same as that in the dome. Furthermore, it was also found that there was no significant difference between intra-aneurysm pressures measured at 2 points on the dome (in Fig. 1. (B)). Table 1 summarizes the obtained values of P_{av} and P_d for the experiment shown in Fig. 2. There was no significant difference between P_d values before and after coil insertion.

3-2. Flow visualization

In Fig. 3 and 4, shown are the flow patterns in the aneurismal models. Before coil insertion, helical flows are clearly observed in the dome as shown in Fig. 3. It should be noted in Fig. 4 that after coil insertion (5 coils occupying 12.7% of the aneurysm volume), dyes tend to stay in a certain intra-aneurismal domain, revealing a lack of strong flow in the aneurysm.

Micro-particles were also utilized to visualize the flow. Complicated helical flows were visualized in the dome before coil insertion. However, after coil insertion, micro-particles showed trembling motion in the aneurysm dome and the helical flows were strongly suppressed. Such flow behavior was found to occur within the Reynolds number range (300 to 600) examined here. These findings indicate that inserted coils can markedly depress intra-aneurysm flow.

3-3. Displacement of aneurismal wall

The elastic aneurismal model was set in the flow circuit described above, and a laser beam from the displacement meter was focused on the top of the aneurysm. Fig. 5 shows the obtained results measured before and after coil insertion. As can be seen, the measured wall displacement showed periodic change due to flow pulsation. It could be noted that the displacement of the wall, which is here defined as a difference between peak and bottom of the wall motion in a pulsation cycle, markedly depressed after the insertion of 7 coils (occupying 17.3% of the aneurismal volume).

In Fig. 6, the measured displacement of aneurismal wall is shown. It could be seen that as the number of coils were increased, the displacement of the wall became smaller. With 9 coils inserted, the displacement decreased to about half of that before coil insertion in this case. A relatively large error bar for the displacement is due to how effectively the inserted coils contact to the aneurismal wall (the measurement was repeated 4-5 times). We also used other 2 silicon models with different wall thickness. The measured wall displacement for these models showed a tendency quite similar to those shown in Fig. 5.

4. Discussion

The mechanism of preventing aneurysm rupture by coil embolization has been explained by ① thrombus formation around inserted coils in response to foreign substances and ② new intimal growth (epithelization) around the neck of the aneurysm[10,11,12,13,14,15].

However, in some cases, neither thrombus formation in the aneurysm nor epithelization around the neck of aneurysm has been observed (especially in patients in the acute phase)[16,17]. Furthermore, densely organized thrombus formation was not observed even 6 weeks after coil insertion in several animal models[18]. These findings suggest that factors other than ① and ② might be involved in the prevention of aneurysm rupture.

We have focused on (1) the buffer effect of coils on blood pressure (2) the flow in the aneurysm and (3) their supporting effect on the aneurismal wall. In this study, glass and silicon cerebral aneurysm models were prepared and used to determine how coil insertion would influence flow and pressure in aneurysms. The results are summarized as follows:

1. Guglielmi detachable coils (GDCs) sequentially inserted into the aneurysm caused no change in intra-aneurismal fluid pressure. As long as fluid remained in the aneurysm, intra-aneurismal fluid pressure was almost the same as the pressure in the proximal vessel. Thus, coil insertion was found to have no buffer effect on intra-aneurismal fluid pressure.

2. Coil insertion strongly obstructed and slowed intra-aneurismal flow. Recently, Imbesi and Kerber have conducted flow visualization in a replica of a lethal wide-neck aneurysm after parent vessel stenting and subsequent intra-aneurismal coiling, and reported that the stent decreased slipstream coherence and placing the coils further disturbed and reduced aneurismal flow[19]. Flow stagnation resulting from coil insertion may facilitate thrombus formation in the aneurysm in late stage. Kaibara, et al cultured endothelial cells on inner surface of a glass model of artery with an aneurismal portion in which the blood was flowed[20]. They reported that the flow stagnation in the aneurysm model promoted thrombus formation in the model.

3. With the increase in number of coils anchored at the aneurismal wall, the displacement of the wall was considerably depressed. Hans, et al have investigated

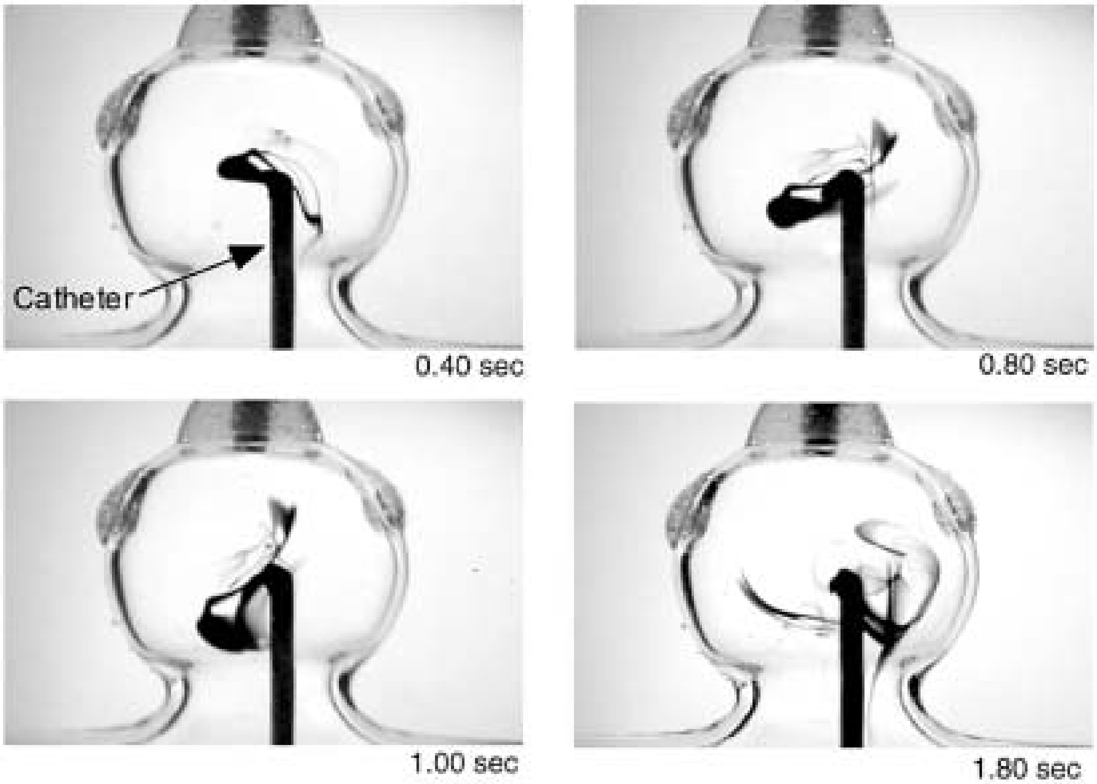

Fig. 3. Flow patterns within the aneuriysmal dome, visualized by isopycnal dye injection: before coil insertion.

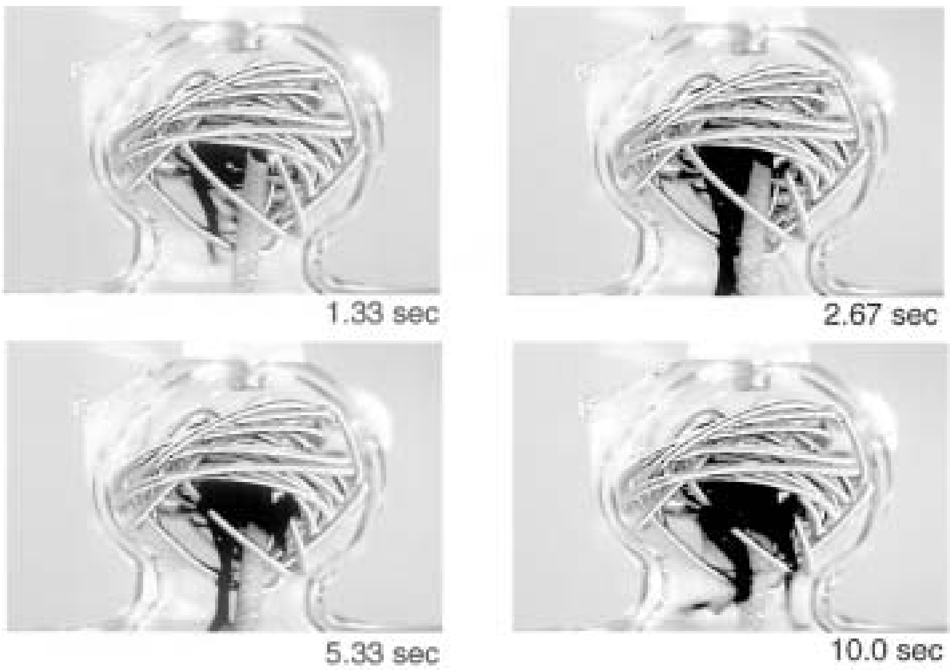

Fig. 4. Flow patterns within the aneuriysmal dome, visualized by isopycnal dye injection: after coil insertion.

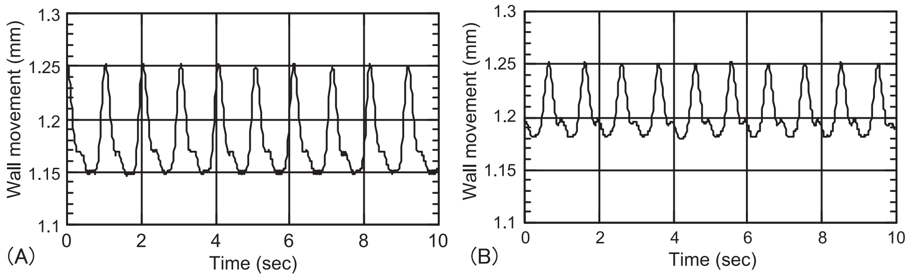

Fig. 5. Aneuriysmal wall movement measured using a laser displacement meter. Panel (A): before coil insertion. Panel (B): after insertion of 7 coils.

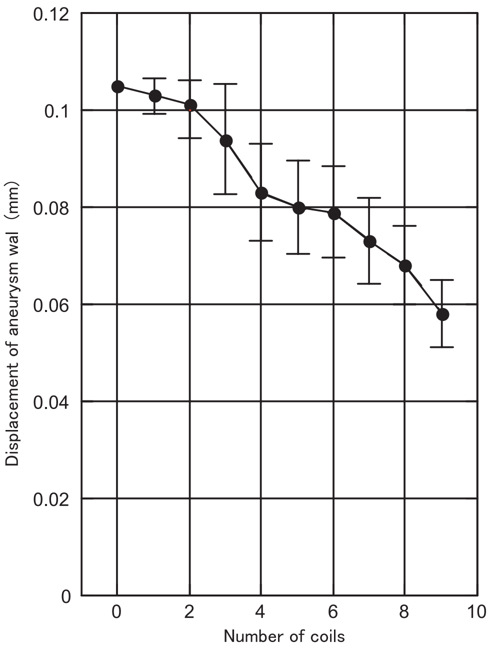

Fig. 6. Maximum wall displacement (the difference between the maximum and minimum wall movement) versus the number of coils inserted into the aneuriysmal dome. Measurements were repeated 4 or 5 times for each data point, and are expressed as the mean. The error bars indicate the maximum and minimum displacement values measured. Statistically significant reductions ($P<0.05$; two-sample Wilcoxon test) compared with the baseline displacement value (measured before coil insertion) were observed when more than three coils were inserted.

the physical effect of coils on flow and pressure dynamics in experimental aneurysms produced by a venous graft technique[21]. They reported that coils did not physically affect intra-aneurismal pressure, but aneurismal wall pulsation might be decreased. Present results of wall displacement by using silicone model support their findings. These results suggest that coil insertion decreases the stress on the aneurysm wall and thereby can prevent aneurysm rupture caused by blood flow pulsation. Steiger, et al investigated the hemodynamic stress in saccular aneurysms and stated that the fluctuations of flow induced vibrations of the aneurismal wall and contributed to aneurysm progression and eventual rupture[22,23,24)].

It is expected that a slight reduction of the wall stress can result in effective protection of aneurysm rupture when the huge repetition of the wall movement due to cardiac pulsation (typically 3600 cycle/hour or 86400 cycle/day) is taken into consideration.

It has been emphasized that the preventive effect of coil embolization on the rupture of cerebral aneurysm is the thrombus formation by tight coil packing in the aneurysm and the endothelial lining around the neck. This study, however, demonstrated that the mechanism of the preventive effect of coil embolization was based primarily on the decrease of the aneurysm wall stress by anchor of coils. Simultaneously, these inserted coils cause flow stagnation and may facilitate thrombus formation in the aneurysm.

In this experiment, the mechanical effect of fibrin or thrombi adhering to coils was not analyzed. If fibrin or thrombi adheres to coils, mechanical interactions between coils and the aneurysm wall are expected to be more strengthened. If coils and the aneurysm wall are glued together by thrombi or other adhesive factors, the aneurysm wall will be moreover strengthened.

5. Conclusions

The present results indicate that the mechanism by which coil embolization prevents the rupture of an intracranial aneurysm may involve the following two factors:

1. Coil insertion depresses the pulsatile aneurismal wall movement, and diminishes the stress of the

aneurismal wall.

2. Coil insertion stagnates intra-aneurismal flow and thereby might facilitates thrombus formation in the aneurysm.

These two factors may display synergistic effects to prevent the rupture of aneurysm.

The present study has demonstrated the mechanical effect of the coil embolization on the aneurysm wall. Procedural improvements and further refinements in devices for coil embolization should be made on the basis of this mechanical effect of coils.

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