

# Creation of Bifurcation-Type Elastase-Induced Aneurysms in Rabbits

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## ABSTRACT

**SUMMARY:** Elastase incubation was performed in the LCCA in 13 New Zealand white rabbits. Three weeks after incubation, DSA demonstrated that 10 (10/13, 77%) bifurcation-type aneurysms at the origin of the LCCA were present; mean aneurysm neck, width, and height values were  $3.7 \pm 1.1$ ,  $3.8 \pm 0.9$ , and  $8.7 \pm 2.3$  mm, respectively. The LCCA can be used to create bifurcation aneurysms in rabbits.

**ABBREVIATIONS:** DSA = digital subtraction angiography; IADSA = intra-arterial digital subtraction angiography; IVDSA = intravenous digital subtraction angiography; LCCA = left common carotid artery; RCCA = right common carotid artery

New Zealand white rabbits have been widely used for creation of RCCA elastase-induced aneurysms,<sup>1-5</sup> which have several advantages over the traditional surgical aneurysms created by using anastomosis between the vein pouch and carotid artery.<sup>1,6-8</sup> Several modifications have been made to the RCCA model to customize resultant aneurysm morphology.<sup>9-11</sup> However, the RCCA model is of sidewall morphology, albeit along a curved vessel and, thus, is limited regarding its use in studying bifurcation-type aneurysm morphologies.

In contradistinction to the RCCA, which originates as a bifurcation with the subclavian artery, the LCCA typically originates as a trifurcation, along with the brachiocephalic artery and the aortic arch.<sup>3</sup> In this study, we applied techniques of aneurysm creation analogous to those used for sidewall RCCA elastase-induced aneurysms to the LCCA and catalogued resultant aneurysm morphology and size.

## DESCRIPTION OF THE TECHNIQUE

### Aneurysm Creation

Elastase-induced aneurysms were created in 13 New Zealand white rabbits, following the approval of our Institutional Animal Care and Use Committee. Anesthesia was induced with an intramuscular injection of ketamine, xylazine, and acepromazine (75,

5, and 1 mg/kg, respectively). Using sterile technique, we exposed and isolated the LCCA. A 1- to 2-mm bevelled arteriotomy was made, and a 5F vascular sheath (Avanti, Cordis Endovascular, Miami Lakes, Florida) was advanced retrogradely in the LCCA to a point approximately 3 cm cephalad to the origin of LCCA. A 3F Fogarty balloon (Baxter Healthcare, Irvine, California) was advanced through the sheath to the level of the origin of the LCCA with fluoroscopic guidance (Advantx, GE Healthcare, Milwaukee, Wisconsin) and was inflated with iodinated contrast material (iohexol, Omnipaque 300; GE Healthcare, Princeton, New Jersey). Porcine elastase (approximately 120 U/mL; Worthington Biochemical, Lakewood, New Jersey) was incubated within the lumen of the LCCA above the inflated balloon for 20 minutes, after which the catheter, balloon, and sheath were removed and the LCCA was ligated below the sheath entry site.

### Imaging Follow-Up

Three weeks following aneurysm creation, DSA was performed, 12 cases through IVDSA and 1 case by IADSA. Details of the IVDSA procedure have been reported previously.<sup>1</sup> Briefly, 7 mL of iodinated contrast material (iohexol, Omnipaque 300) was injected into the left ear vein through an angiocatheter at approximately 2 mL/s. For IADSA, a right femoral artery cutdown was followed by 5F catheter inserted into the aortic arch, followed by injection of 5 mL of contrast (Omnipaque 300). The x-ray exposure rate was 2 frames per second.<sup>12</sup> 3D DSA was also performed in 4 cases by using the Artis Zee fluoroscopy system (Siemens, Erlangen, Germany), which involves a 5-second 200° rotation with acquisition of 133 images during 20 mL of contrast injection (Omnipaque 300, injection rate 4 mL per second) in the ascending aorta.<sup>13</sup> Original 3D rotational images were reconstructed and displayed by using a volume-rendering technique.

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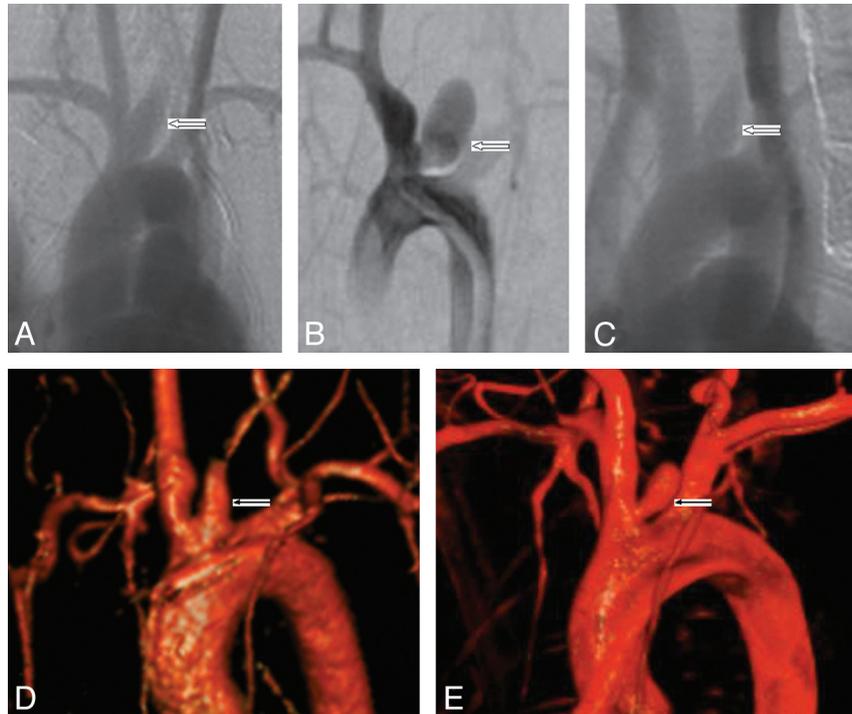
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**FIG 1.** A–C, Anteroposterior IVDSA images show 3 bifurcation aneurysms (*black arrow*). D and E, 3D DSA images show 2 aneurysms located in the bifurcation between the aortic arch and brachiocephalic trunk (*black arrow*).



**FIG 2.** Anteroposterior (IVDSA) image shows a sidewall aneurysm originating from brachiocephalic trunk only (*black arrow*).



**FIG 3.** Anteroposterior IADSA image shows another sidewall aneurysm originating from aortic arch (*black arrow*).

Patent saccular aneurysmal structures were present in all cases, with bifurcation-type aneurysm morphologies in 10 (77%) of 13 rabbits (Fig 1). A “bifurcation-type aneurysm” was defined as an aneurysm that originated exactly from the angle between brachiocephalic trunk and the aortic arch. Two (15%) cases showed the LCCA aneurysms originating from brachiocephalic trunk alone, with resultant sidewall aneurysm morphology (Fig 2), and 1 (8%) sidewall aneurysm originated from the aortic arch directly (Fig 3).

The width, height, and neck diameters of the aneurysm cavities were determined and calculated by using IVDSA images with the external sizing device as a reference. The mean aneurysm neck

size was  $3.7 \pm 1.1$  mm (range, 2.1–6.5 mm). The mean aneurysm width was  $3.8 \pm 0.9$  mm (range, 2.6–5.9 mm). The mean aneurysm height was  $8.7 \pm 2.3$  mm (range, 7–14 mm).

## DISCUSSION

In this study, we modified the typical rabbit elastase-induced aneurysm model by ligating and injuring with elastase the left, rather than right, common carotid artery. As a result, the large majority of resultant aneurysms demonstrated bifurcation anatomy rather than the typical sidewall morphology in the RCCA model. A small

number of subjects showed sidewall aneurysm morphology, arising from either the brachiocephalic trunk or the aortic arch.

Bifurcation aneurysms are exposed to different hemodynamic features compared with sidewall aneurysms.<sup>14</sup> They are more common than sidewall aneurysms in patients with intracranial aneurysms, including aneurysms that originate from the bifurcation of the internal carotid and posterior communicating arteries, and the middle cerebral artery bifurcation. Compared with the sidewall aneurysm model, the bifurcation aneurysm shows more encouraging results for evaluation of neurovascular devices.<sup>15,16</sup> Studies involving computational fluid dynamics simulations also use the bifurcation aneurysm as an important tool.<sup>17</sup> Thus, this study will expand the application of the elastase-induced aneurysm model to investigate the physiology of bifurcation aneurysms and test endovascular devices aimed at treating bifurcation-type aneurysms.

Elastase-induced aneurysms have previously been created from the LCCA,<sup>18</sup> in which the aneurysms were created by using transfemoral endovascular means with distal LCCA occlusion by using detachable balloons or coils; elastase injury was achieved from an endovascular approach that was time-consuming and associated with substantial morbidity. The current study offers a practical, simple direct surgical exposure method, which is similar to that widely applied for RCCA aneurysm creation.

This study had a small sample size. Further study regarding this issue is being done to validate this model.

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