

## SHORT REPORT

## Onyx Migration Into the Anterior Spinal Artery During Lumbar Artery Embolisation: an Adverse Event

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**Introduction:** The impact of sequential lumbar and intercostal artery occlusion on the risk of spinal cord ischaemia was evaluated; however, an adverse event (paraplegia) was encountered, which resulted in study interruption. Investigations were carried out to understand the reasons for the paraplegia.

**Report:** To develop a porcine model of spinal cord ischaemic preconditioning prior to extensive thoraco-abdominal aneurysm endovascular aortic repair, the lumbar arteries were selectively embolised with Onyx 5 days prior to an extended thoracic aortic stent graft. Six pigs were used in this preliminary work. Four cases of paraplegia secondary to accidental migration of Onyx to the anterior spinal artery from the lumbar arteries are reported. Histological analysis confirmed severe spinal ischaemic injury and the presence of Onyx particles in the anterior spinal artery.

**Discussion:** Onyx is used for lumbar artery embolisation in type II endoleak treatment after endovascular aortic repair, and while migration in lumbar arteries is frequent, the risk of spinal cord ischaemia has never been described. The current study demonstrates the risk of paraplegia following Onyx migration to the anterior spinal artery from the lumbar artery in an experimental model. Thus, Onyx treatment for type II endoleaks from lumbar arteries should be used cautiously.

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### INTRODUCTION

The risk of spinal cord ischaemic injuries during thoracic endovascular aortic repair (TEVAR) persists despite several preventive strategies and is seen in 3–5% of patients.<sup>1</sup> Spinal cord preconditioning has been used to prevent the neurological impact of spinal ischaemia—reperfusion injury related to aortic procedures.<sup>2,3</sup> Initially, a strategy to minimise the risk of spinal cord injury after extensive thoraco-abdominal aneurysm repair was evaluated. It was hypothesised that blood flow disturbances induced by previous lumbar artery embolisation with ethylene vinyl alcohol copolymer (Onyx) would lead to microvascular remodelling and arteriogenesis.<sup>4</sup> Indeed, many studies support the existence of multiple connections into the anterior spinal artery and this impressive collateral network is able to increase blood flow to the spinal cord when one or other source is reduced.<sup>2,3</sup> Therefore, an improvement in

post-operative neurological outcomes after extended thoracic aortic coverage was expected.

Herein, four cases of complete paraplegia secondary to accidental migration of Onyx to the anterior spinal artery from the lumbar arteries are reported.

### REPORT

The Aix-Marseille University Ethical Committee on Animal Experimentation (no. A-13-05532) approved all experiments. All procedures were performed under general anaesthesia.

Six adult Pietrain pigs weighing a mean  $\pm$  SD of 59.8  $\pm$  1.2 kg were used.

On day 1, after a surgical approach to the right femoral artery, the lumbar segmental arteries (SAs) were catheterised and embolised bilaterally in the cranio-caudal axis with Onyx (0.2–0.5 cc) from the L5 to the L1 level. Embolisation success was confirmed by selective angiography of the trunk of each artery. On day 5, intercostal SAs were occluded by thoracic endovascular stent grafting. Motor evoked potentials were measured in the lower limb during surgery and at the end of each procedure. Hindlimb function was evaluated daily using a modified Tarlov score (0 = paraplegia, 9 = full recovery).<sup>2</sup> Each animal was videotaped.

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Animals with a modified Tarlov score  $<7$  at the end of the protocol were considered to have sustained significant spinal cord damage (paraplegia/paraparesis).

At day 10, all animals were euthanised, and the spinal cord was surgically harvested.

These results should be compared with a similar group of animals that underwent the same extent of SA sacrifice in a single stage.

After the animals were sacrificed, the spinal cord was surgically harvested, fixed in 10% formalin solution and sliced in sections transverse to the cranio-caudal axis. Sections, 5  $\mu\text{m}$  thick, were stained with hematoxylin and eosin, examined, and scored blindly by an experienced neuropathologist according to a schematic grading system (Kleinman score).<sup>3</sup> Five to 10 slices were performed at each level.

Six animals in group 1 (sacrificed in two stages) survived the first endovascular procedure, but in four of the six pigs a paradoxical complete post-operative paraplegia (Tarlov score 1) was diagnosed during and after the first arterial embolisation sequence. None regained normal spinal cord function and these four pigs were prematurely euthanised. Macroscopic examination of the spinal cord revealed the presence of Onyx in distal segmental spinal arteries and in the anterior spinal artery (Fig. 1A). These findings were confirmed by a computed tomography scan of the harvested spinal cord (Fig. 1B). Histological analysis of the spinal cord confirmed the presence of Onyx in the anterior spinal artery (Fig. 2A–C), and ischaemic injury was detected in four pigs. The lower thoracic and abdominal segments showed severe and diffuse signs of spinal cord injury, with neuronal necrosis present in both the posterior and anterior gray horns (Fig. 2D). Neuronal necrosis was found from the T8 to the L4 levels, and the lower thoracic and the

abdominal segments presented severe and diffuse signs of spinal cord injury, often including complete necrosis of an entire section and involving several adjacent segments (Fig. 3).

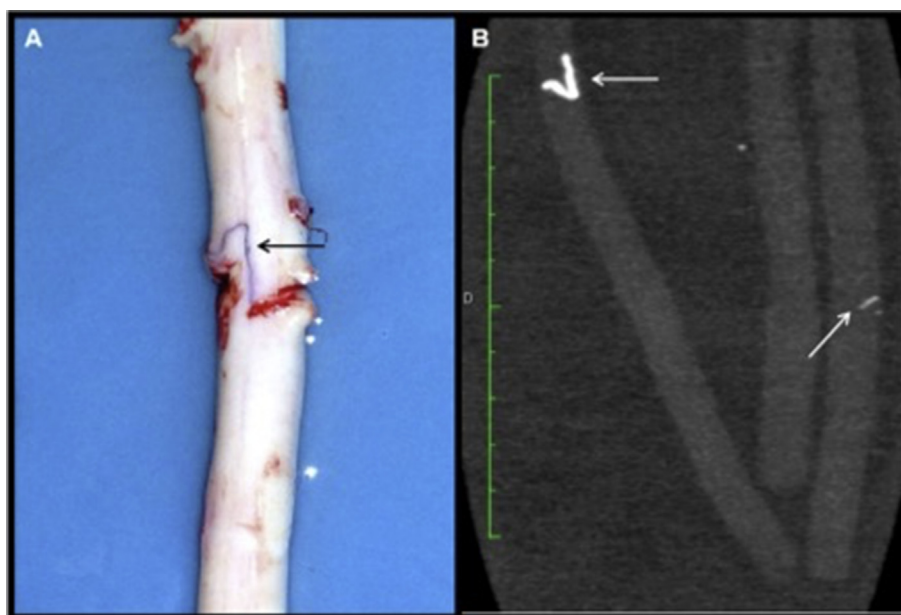
Owing to these unexpected adverse events, the use of Onyx was suspended. Lumbar artery coiling was used for later experiments.

## DISCUSSION

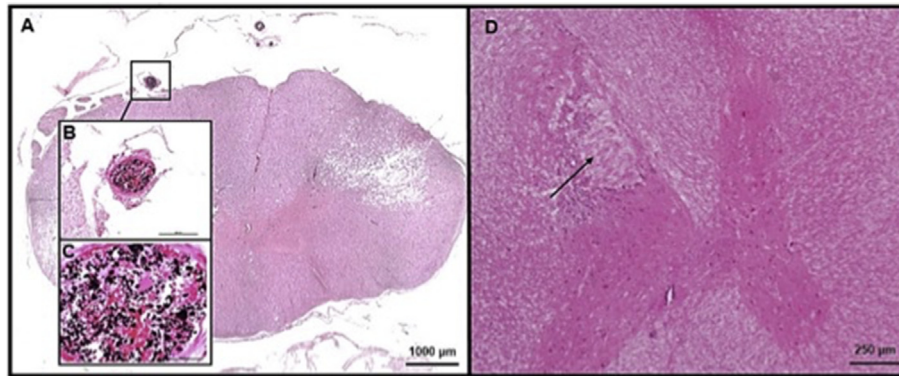
In this experimental study to evaluate the preconditioning effect of prior selective embolisation of segmental lumbar arteries on spinal cord ischaemia–reperfusion injury after TEVAR, severe spinal infarcts due to the accidental migration of the embolisation material (Onyx) in the distal spinal circulation, were found. Indeed, two thirds of the animals included in this preliminary work showed this adverse event. Interestingly, Onyx spinal migration and neuronal injury were detected cranially and relatively far from the level of the embolisation, highlighting the migratory capacity of this liquid agent.

The choice of Onyx as the embolisation agent was initially made for several reasons. First, the excellent cohesive properties of Onyx should have prevented distal migration.<sup>5</sup> Second, embolisation with a liquid material is technically easier and requires a less stable catheter position than solid materials such as coils. In the clinical context of thoraco-abdominal aneurysms, selective segmental arterial catheterisation may be difficult. Therefore a liquid material was chosen in anticipation of potential clinical use.

On an experimental note, this report does not eliminate the plausible preconditioning effect of prior selective embolisation of lumbar SAs, a hypothesis supported by several



**Figure 1.** (A) Macroscopic view of the harvested spinal cord showing the presence of Onyx in a distal segmental spinal artery and in the anterior spinal artery (black arrow). (B) Computed tomography scan of the spine confirming multiple locations of Onyx particles (white arrows).



**Figure 2.** (A) Microscopic transverse view of the spinal cord and the anterior spinal artery at the T10 level. (B, C) Onyx particles are visible in the anterior spinal artery. (D) Neuronal necrosis is localised to the right anterior gray horn at the T10 level (black arrow).

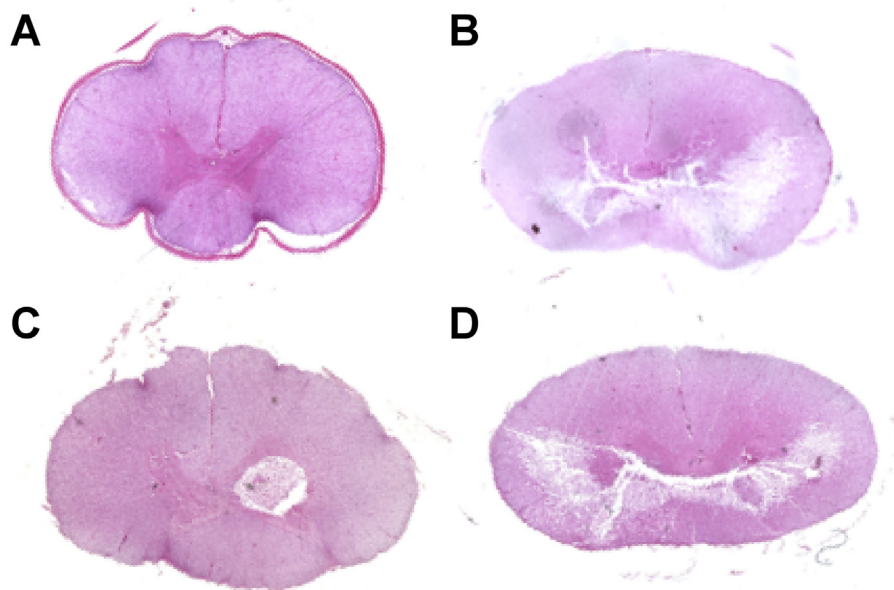
studies.<sup>2,3,6</sup> However, the use of Onyx in this specific animal model should be abandoned.

On a clinical note, Onyx is regularly used in vascular surgery for the treatment of type II endoleaks after endovascular aortic repair. Type II endoleaks after endovascular aneurysm repair are a common complication with incidence rates of up to 20%.<sup>7</sup> Several methods of endoleak management have been proposed. Approaches include transarterial management and embolisation of the inflow and outflow arteries through the arc of Riolan or the hypogastric–lumbar junction, transcaval puncture into the aortic sac, or direct translumbar or trans-abdominal puncture of the aneurysm sac. Onyx is one material used in this situation, as it is technically difficult to embolise the ostium of the artery with a coil. The risk of distal Onyx migration from lumbar arteries remains theoretical; indeed, while migration in lumbar arteries is frequent, the risk of spinal cord ischaemia has not been described in humans. The

current literature lacks data regarding the use of Onyx as a monotherapy to treat endoleaks.

This report shows that migration of onyx into the lumbar arteries could expose patients to the risk of spinal cord ischaemia.

Anatomical and haemodynamic differences in the segmental aortic arteries and spinal circulation between the native pig aorta and the aneurysmal human aorta cannot be excluded, but the relevance of these findings to the clinical situation is supported by numerous previous physiological studies in which patterns of response in the pig model have proved remarkably similar to observations in patients with aortic disease.<sup>8–10</sup> The injection of Onyx directly into the lumbar arteries differs from the clinical situation in humans, when Onyx is often injected in the aneurysm sac. The blood flow in a non-treated aneurysm is different to that in a endovascularly treated aorta (in a type II endoleak situation the flow is reversed). Then, the risk of spinal artery migration is potentially lower.



**Figure 3.** Microscopic transverse view of the spinal cord. (A) T6 level: normal spinal cord. (B, D) T12/T13 level: necrosis of both anterior and posterior horns, as well as white matter (8/8 Kleinman score). (C) L2 level: central necrosis involving the posterior and anterior horns plus parts of the white matter (6/8 Kleinman score).

Nonetheless, this report should be of great interest to vascular surgeons, and the cautious use of Onyx for type II endoleak embolisation is suggested, particularly in cases of type II endoleak from lumbar arteries.

Onyx is used for type II endoleak treatment after endovascular aortic repair, and while migration in lumbar arteries is frequent, the risk of spinal cord ischaemia remains unclear and has not been described in humans. The current study demonstrates the risk of paraplegia following Onyx migration to the anterior spinal artery from the lumbar artery in an experimental model. Thus, Onyx treatment for type II endoleaks from lumbar arteries should be used cautiously.

#### CONFLICTS OF INTEREST

None.

#### FUNDING

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