Onyx (Covidien, Irvine, California) was initially manufactured as a dialysis matrix for separating immunoglobulin from albumin and then as a matrix for controlled release of chemotherapeutics. However, it was also found to have embolic properties, and its clinical use for this purpose was first described in 1990 for embolization of intracranial arteriovenous malformation (AVM). At that time, Onyx showed promising results, overcoming the drawbacks of cyanoacrylate, a well-known embolic liquid agent commonly used for the same purpose. The lack of adhesiveness and slow copolymerization rate permit more distal nidus embolization, sometimes including the proximal venous outflow, without significant risk of microcatheter entrapment. After several studies, including a multicenter randomized trial comparing Onyx and cyanoacrylate, in July 2005, the U.S. Food and Drug Administration approved its use for intracranial AVM embolization. European device approval (CE marking) preceded that in the United States by approximately 5 years for embolization of AVMs and intracranial aneurysms as well. Since then, given the safety and effectiveness of Onyx in the intracranial vasculature, use on peripheral organs has been described and successfully applied. Nowadays, it has been used mainly for the treatment of peripheral AVMs and abdominal aorta stent graft–related endoleaks. In addition, Adams et al. published a series of cases describing 23 patients in whom Onyx embolization was successfully performed, including treatment of the renal, hepatic, iliac, and bronchial arteries and esophageal varices. The authors concluded that Onyx offers advantages over other embolic agents due to good controllability and faster vessel occlusion.

DEVICE/MATERIAL DESCRIPTION

Onyx is a liquid permanent embolic agent composed of ethylene vinyl alcohol (EVOH) copolymer dissolved in dimethyl sulfoxide (DMSO) and micronized tantalum powder. The latter provides contrast for fluoroscopic visualization. The nonadhesive and viscous properties make it a unique agent, mostly differing from the other two known liquid embolic agents—glue and dehydrated alcohol. Its nonadhesive characteristic significantly decreases the risk of microcatheter entrapment, compared to glue (Table 10.1). The higher viscosity allows controlled deployment, which is extremely difficult to achieve with dehydrated alcohol.

The Onyx package includes three 1-mL delivery syringes, two labeled for Onyx use (white plunger) and one for DMSO (yellow plunger); one 1.5-mL vial of Onyx; and one 1.5-mL vial of DMSO (Fig. 10.1). The Onyx white plunger syringe has lower friction compared to the DMSO yellow one, which gives better control while the agent is being injected. DMSO is a solvent and is used to wash out the microcatheter and prevent immediate direct contact between Onyx and the bloodstream, which ultimately triggers the solidification. Because of the theoretical risk of melting down non–DMSO-compatible microcatheters, it is recommended using only pretested microcatheters, including Marathon, Rebar, Echelon, and UltraFlow (Covidien, Irvine, California). They have been extensively tested regarding their compatibility with DMSO, which is outlined further in Chapter 12. In addition, their dead space volume is provided in the microcatheter package (dead space: volume necessary to fill up the lumen of the microcatheter completely).

Three different Onyx viscosities are available with different EVOH concentrations: Onyx 18 (with 6% of EVOH),
Embolic Materials ■ Liquid Agents

Table 10.1
Comparison between Onyx and Cyanoacrylate (Glue) Regarding Mechanism of Action, Preparation, and Administration

<table>
<thead>
<tr>
<th>Onyx</th>
<th>Glue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to solidification</td>
<td>4–5 min</td>
</tr>
<tr>
<td>Injection time</td>
<td>Several minutes</td>
</tr>
<tr>
<td>Adhesiveness</td>
<td>Low</td>
</tr>
<tr>
<td>Final consistency</td>
<td>Foamlike substance</td>
</tr>
<tr>
<td>Microcatheter compatibility</td>
<td>Restricted</td>
</tr>
<tr>
<td>Preparation</td>
<td>20-min shaking</td>
</tr>
<tr>
<td>Solidification process</td>
<td>Copolymerization</td>
</tr>
<tr>
<td>Preembolization flushing</td>
<td>DMSO</td>
</tr>
</tbody>
</table>

*It will depend on the glue concentration.


Onyx 34 (with 8% of EVOH), and Onyx 500 (recommended for giant intracranial aneurysms). The second formulation is almost twice as viscous as the first one. Higher viscosity (Onyx 34) offers better control while the embolic agent is injected, but as the copolymerization process is faster, agent delivery in areas too distal to the microcatheter tip is more difficult. Therefore, this formulation is best suited for very high-flow lesion, with important vascular branches that must be preserved, and when the microcatheter tip is close or within the target lesion. On the other hand, a lower viscosity formulation (Onyx 18) is preferred when the microcatheter cannot be advanced any closer to the lesion and the target area is still too far away from the microcatheter tip. The lower viscosity and slower copolymerization time allow the liquid embolic agent to flow deeper, reaching more distal areas of the lesion. As one can note, it is usually a trade-off between a more controlled delivery but with less chance of full lesion embolization or complete lesion embolization with higher risk of occlusion of nontarget vessels.

Another unique Onyx characteristic is the “outside-in” solidification process. First, the outer layer forms a solid cast while a spongy or foamlike consistency is created inside, similar to what happens to the volcano lava when it cools off. The solidification process, also called copolymerization, starts once Onyx comes in contact with ionic fluids, such as blood, iodine contrast material, and saline solution, and usually takes 5 minutes to reach a solid and stable consistency. In contrast to dehydrated alcohol that causes an acute and severe endo- thelitis, Onyx induces a mild inflammatory reaction in the adjacent vessel walls, and as a nonabsorbable embolic agent, recanalization of the embolized area is nonexistent.9

**CLINICAL APPLICATIONS IN PERIPHERAL EMBOLIZATIONS**

Early report on peripheral Onyx application date back to 2001, when Martin and colleagues6 reported Onyx embolization of endoleak types II and Ia. All patients presented with decreased aneurysmal sac diameter after a mean follow-up of 19.2 weeks.6 Since then, multiple reports have been published, describing successful Onyx embolization for different pathologies among different peripheral vascular territories, including visceral aneurysms; pseudoaneurysms; hemoptysis; gastrointestinal bleeding; and abdominal, pulmonary, and upper and lower extremity AVMS.4,5,10–13 For all these entities, Onyx has been shown to be as useful as other conventional embolic agents or sometimes even more effective due to faster vessel occlusion and good delivery control.8 Moreover, Onyx can be considered the embolic agent of choice for peripheral AVMs and type II endoleak embolization.14

Typically, AVMs are challenging lesions to be treated due to the combination of potential high-flow environment and the need for distal intranidus embolization. As a liquid embolic agent, Onyx can reach small vessels deep within the nidus, sometimes far away from the delivery microcatheter. At the same time, different predictable viscosities allow safe agent delivery with low risk of distal nontarget embolization (Fig. 10.2).

With a similar flow dynamics, type II endoleaks can behave like AVMs, having the aneurysmal sac as a functional “nidus,” associated with multiple inflow and outflow vessels. In this scenario, Onyx has been shown as an extremely efficient embolic agent, achieving complete filling of the open channels within the aneurysmal sac and also proximal occlusion of the involved vessels (Fig. 10.3).
**Figure 10.2**  
A: Selective inferior mesenteric arteriogram showing arteriovenous shunting through a nidus overlying the distal descending colon, associated with multiple feeding vessels and dilated drainage veins.  
B: Superselective catheterization of one of the feeding vessels and positioning of the catheter “facing” the nidus.  
C: Control arteriogram postembolization demonstrating the cast of Onyx filling portion of the nidus and feeding vessels. There is marked reduction of flow shunting.

**Figure 10.3**  
A: After obtaining translumbar access to the abdominal aortic aneurysmal sac under computed tomography guidance, the patient was brought to the angiography room and an initial image was acquired with hand contrast injection through a KMP catheter. Note the filling of the aneurysmal sac and retrograde opacification of hypertrophied lumbar arteries.  
B: Completion image after occlusion of the lumbar artery with coils and Onyx embolization of the aneurysmal sac. Note the extensive embolization achieved with Onyx due to its spreadability, making possible occlusion of gaps away from the delivery catheter.
As noted, Onyx is a versatile embolic agent with a broad clinical application, therefore it should be part of any interventionalist’s armamentarium. Comprehensive knowledge of agent properties and delivery technique are essential for an efficient and safe embolization. Peripheral use of Onyx is a field yet to be fully explored, and for that, familiarity with the technique is fundamental.

**TECHNIQUE**

To obtain a homogeneous Onyx solution, ensuring easy delivery and good opacification, the vial of Onyx has to be shaken for at least 20 minutes before the Onyx is aspirated into the delivery syringe. Therefore, to avoid delay, shaking process using an automatic system should start while access to the target lesion is obtained (Fig. 10.4). After proper positioning of the diagnostic catheter, a Tuohy Borst adapter (Cook Medical) is connected to the catheter hub, and coaxially, a microcatheter is advanced up to the target zone.

Hand iodine contrast injection is performed to check the working position and system stability. Ideally, the microcatheter should be as distal as possible, “facing” the lesion (see Fig. 10.2B). In situations where the microcatheter cannot be advanced closer to the lesion, which might be 1 or 2 cm away from the tip, a less viscous solution (Onyx 18) should be selected, as explained earlier.

Again, according to the manufacturer, only DMSO-compatible microcatheters should be used, and these include the Marathon, Rebar, Echelon, and UltraFlow. It is important to notice that the Marathon and UltraFlow microcatheters are flow-directed catheters with very small inner diameters, allowing maximum 0.010-in guidewires. This implies less maneuverability, which can impose difficulty when dealing with complex anatomy, with increased tortuosity and multiple branching vessels.

When in proper position, the microcatheter is washed out with normal saline and slowly filled up with DMSO. The microcatheter dead space volume is available on the package label. DMSO in high concentration can cause acute irritation to the endothelium, leading to painful sensation. So, if the patient experiences pain at this point, it means too much DMSO has been injected, above the dead space limit, or it has been injected too fast, not allowing enough time for the DMSO to mix with the blood. Because DMSO is not radiopaque, fluoroscopy is not necessary during catheter filling. Overwashing the microcatheter hub with residual amount of DMSO will prevent triggering of the copolymerization process while the Onyx solution is still inside the catheter, avoiding its occlusion. At this point, the Onyx syringe should be already filled.

Aspiration of the microcatheter before Onyx injection is not permitted. Therefore, to avoid presence of air bubble within the catheter, connection of the Onyx syringe to the microcatheter hub should be done in a vertical position, and a drop of Onyx may be necessary to fill up a residual gap within the microcatheter hub (Fig. 10.5). Onyx must always be injected slowly, since the very first time, allowing

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**Figure 10.4** Picture of the automatic shaker used to obtain a homogenous Onyx solution before aspiration into the delivery syringe. The vials are placed on top of the machine, and the shaking process should last at least 20 minutes. To avoid time wasting, shaking process should start while access to the lesion is being obtained.

**Figure 10.5** Note the vertical position of the microcatheter and the Onyx syringe when both are being attached. At this time, a small amount of Onyx is dropped into the catheter hub to fill any air gap, avoiding bubbles within the system.
adequate and asymptomatic dilution of the DMSO column within the bloodstream. If the patient complains of pain, the injection rate should be slowed down because Onyx is displacing DMSO too fast into the blood vessel, leading to endothelium irritation as mentioned earlier.

Usually, a cast of Onyx in front of the microcatheter forms fast, with a tendency of retrograde flow toward the body of the microcatheter. Although Onyx is not an adhesive agent, the catheter can get stuck within the vessel due to increased extrinsic compression by the “plug” around the microcatheter. For this reason, excessive retrograde flow along the microcatheter body should be avoided. Also, small arteries have low compliance, leading to higher pressure around the catheter and therefore increasing the risk of having the microcatheter entrenched within the vessel.

However, a stable plug around the catheter tip is very useful as it prevents any further retrograde Onyx flow. Therefore, the goal is to create a plug around the tip of the microcatheter, with sufficient amount of Onyx that can prevent retrograde flow but not too much that can increase the risk of catheter entrapment. Hence, no more than 1 to 1.5 cm of Onyx is allowed to move back along the tract of the microcatheter. If too much vessel tortuosity is present, that length should not exceed 0.5 cm (Fig. 10.6). Once the plug is well organized, it will prevent further backflow of the embolic agent, and the Onyx is then delivered only forward in relation to the microcatheter tip. This is called the plug technique, and for obvious reasons, it is unnecessary when there is free anterograde flow in the vessels, such as in portal vein embolization.

Depending on the capacity of the target lesion, large amount of Onyx may be required. The syringes should be simply exchanged, avoiding gaps and without additional DMSO injection. Several minutes or multiple Onyx injections might be required to obtain satisfactory embolization. Rate of infusion is defined by careful observation of Onyx behavior within the target area, which depends on the blood flow and vessel capacity. The gap between injections should be minimal to keep a continuous column of Onyx, with constant forward flow toward the target zone. This will achieve a larger embolized area with less risk of nontarget embolization as flow redirection by solidified Onyx is less likely to occur.

Due to Onyx radiopacity and complex configuration of most of the lesions, it may be difficult to visualize in which direction the agent is being delivered in a posteroanterior or even in oblique views as the previously injected Onyx might obscure the microcatheter. At this point, road mapping should be used to subtract from the image the Onyx that has been already delivered, allowing visualization of the Onyx that is being currently injected. In that way, it is possible to obtain full control and visualization during injection. Successive road mappings may be performed repeatedly every time there is a compromise in Onyx delivery visualization. However, the most important limitation of this technique is the respiratory-dependent artifact, which blurs the road mapping image. Thus, although this technique is extremely helpful when treating intracranial or extremity lesions, its use is limited when working in the abdomen or chest.

After satisfactory embolization of the target area, the entry point of the lesion may be blocked by slow retraction of the microcatheter while Onyx is gently injected, leaving a “tail.” In theory, this technique helps isolate the lesion and prevents further inflow from that particular feeding vessel. This can be applied in endoleaks type I or II and pedicles of AVM nidus. Any inadvertent microcatheter pulling may lead to loss of delivery control and possible nontarget embolization.

Microcatheter removal should be done by applying negative pressure through the delivery syringe and without much effort, giving the nonadhesive nature of Onyx. If resistance is present due to excessive external compression, continuous small increments in the traction intensity should be small.

![Figure 10.6](image)

**Figure 10.6**

**A:** Schematic drawing demonstrating selective catheterization of straight feeding vessel (red) and the microcatheter facing the target lesion. In this situation, the Onyx plug (black) can be as long as 1.5 cm along the catheter’s tip (blue). **B:** Schematic drawing of a different situation where the feeding vessel (red) has significant tortuosity. Again, the microcatheter is facing the lesion, and at this time, the Onyx plug (black) should not exceed 0.5 cm along the microcatheter’s tip (blue).
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DMSO injection should be performed while the balloon is deflated to avoid accumulation of DMSO within the sac, which can dilute the Onyx solution, leading to a longer or unpredictable copolymerization time. Therefore, the balloon should be inflated just before Onyx delivery and with a very diluted iodine contrast solution to avoid obscuring the area of interest. Usually, 4 or 5 minutes are enough to complete the solidification process, allowing safe balloon deflation.

POTENTIAL COMPLICATIONS

Onyx embolization has the same complications as embolization with other embolic agents, which is basically nontarget embolization. To avoid that, superselective catheterization, appropriate application of the plug technique, and correct choice of agent viscosity are key factors. Despite the non-adhesive characteristic, there is potential risk of having the catheter stuck within the vessel due to excessive external compression around the catheter’s tip. As described earlier, to prevent that, the plug should not exceed 1.5 cm in length, and if a lot of tortuosity is present, 0.5 cm should be the maximum plug extension. A common side effect is the garlic-like smell that the patient presents the day after the procedure. That is related to DMSO metabolization and usually resolves after 2 days.

Figure 10.7  A: Right femoral arteriogram demonstrates pseudoaneurysm originating from a branch of the profunda femoral artery. Note the two small branches coming off the lesion itself. B: After coil embolization of the two small branches coming off the pseudoaneurysm, the sac and parent vessel were occluded with Onyx, whereas protection of the profound femoral artery was accomplished with an inflated angioplasty balloon. Note the parallel disposition of the microcatheter used to deliver the embolic agent and the angioplasty balloon. C: Completion arteriogram demonstrating complete exclusion of the pseudoaneurysm from the circulation and preserved flow in the profound femoral artery. (From Guimaraes M, Wooster M. Onyx [ethylene-vinyl alcohol copolymer] in peripheral applications. Semin Intervent Radiol. 2011;28[3]:350–356.)
TIPS AND TRICKS

- Onyx needs to be shaken for at least 20 min. It is important to start the shaking process while access to the lesion is being obtained.
- Use only DMSO-compatible microcatheters. DMSO will not affect the microcatheter structure. Also, the microcatheter dead space volume is available in the package label.
- DMSO should be injected slowly. If the patient complains of pain during the injection, either the dead space volume was overestimated or the hand injection rate is too high (inadequate time for dilution with blood).
- The residual DMSO volume, after the dead space injection, should be used to overwash the hub to avoid any air bubble at the back of the syringe.
- If the microcatheter tip is far away from the nidus (in AVMs) or from target lesion, consider Onyx 18. If it is close to the target or if it is desired to have better control during the injection, consider Onyx 34. Onyx 500 is typically used for giant aneurysms.
- Once Onyx is injected through the microcatheter tip, attention should be paid on the reflux toward the hub of the microcatheter. It is desired to form a short plug around the tip that will allow further injection of Onyx to be pushed forward.
- Differently than glue, Onyx may be slowly injected for several minutes as long as adequate plug is formed and there is no interruption in the column of Onyx injection.
- Onyx occupies free space by sedimentation; it does not polymerize like glue. However, microcatheter tip still can get trapped if the plug created around the tip gets too long (>2 cm).
- In case the microcatheter tip gets trapped, it typically will come out if a gentle, continuous pullback is applied from the hub of the microcatheter. Avoid sudden and intense pullback.

REFERENCES