GLUBRAN®2 for endovascular use: indications and techniques

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HOW TO BECOME GLUE CONFIDENT

MediMay COMMUNICATION

GEM SOLUTION COMES FROM EVOLUTION.

Index

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Presentation

Most interventional radiologists see the use of glue as a practice that can lead to multiple complications, chiefly the risk of the catheter sticking to the vessel and generating non-target embolization.
During this training, some useful advice will be offered towards performing a safe and proper embolization, helping the radiologist to avoid such risks.

This booklet wants to be an accessory of this hands-on course on the use of the glue Glubran®2 as liquid embolizing agent. It has been created with the dual purpose of supporting the trainee during the theoretical part of the training and of releasing basic information, instructions, tips and tricks the Radiologist can consult before starting the first experiences of embolization with “glue” independently.

Prof. **Romaric Loffroy**

GLUBRAN®2

ENDOVASCULAR

SOLVES.

Building the perfect Embolization

GEM SOLUTION COMES FROM EVOLUTION.

Introduction

Embolic agents

Embolic agents can be classified into solids, particles and liquids. Solid agents that can be positioned at target site include coils and microcoils, plugs, and balloons. Agents to be released in the bloodstream can be sub-categorized into *particles* and *liquids:* particles can be absorbable or non-absorbable, spherical or non-spherical; liquid agents include cyanoacrylates, gelling solutions, and sclerosing agents (Fig.1). While indications such as varicocele respond well to any kind of treatment, others, such as lower gastrointestinal (GI) bleeding, offer a restricted choice, as the radiologist may have to reach a very distal vessel by using means of a small microcatheter.

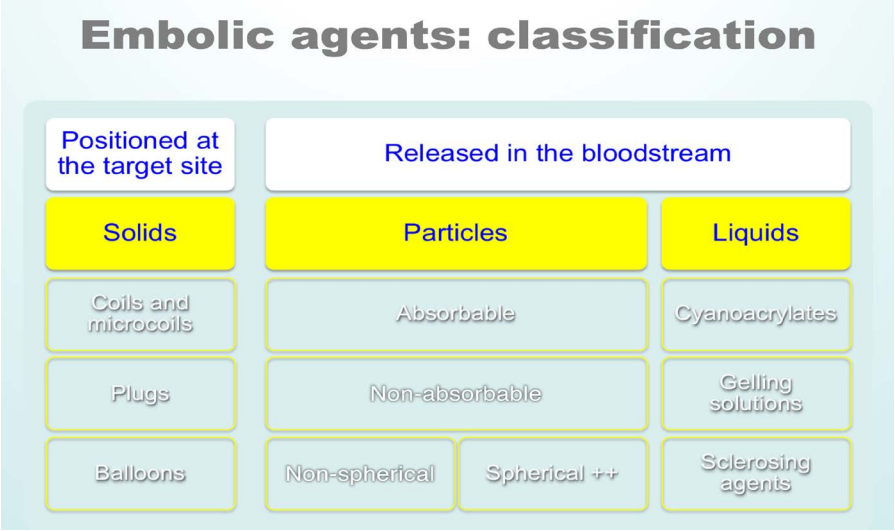


Figure 1

In such cases, liquids are often the best solution, as it may be difficult to properly deploy solid agents, even when it comes to small microcoils (Fig.2). On the contrary, injecting liquid is a viable option in any kind of indication. An interventional radiologist needs to be able to master every tool at their disposal. Gelling solutions or coils can prove efficacious in many cases, however, some indications require a combination of liquid and solid agents or, as this presentation will show, sometimes glue simply represents the best option. The oldest cyanoacrylate for endovascular use is Butyl (NBCA), known as Histoacryl® in Europe and Asia, and Truefill® in the United States. Although Histoacryl® is normally employed in endovascular use, it is never commercially promoted as a product suitable for this kind of environment as it lacks official approval. Truefill® has FDA approval, however, it is only available in the US. The lack of a CE marking is not the only downside to employing Histoacryl®. As one of the most common causes for complications is dried glue causing the microcatheter to stick to the vessel, quick polymerization may increase such risk (Fig.3).

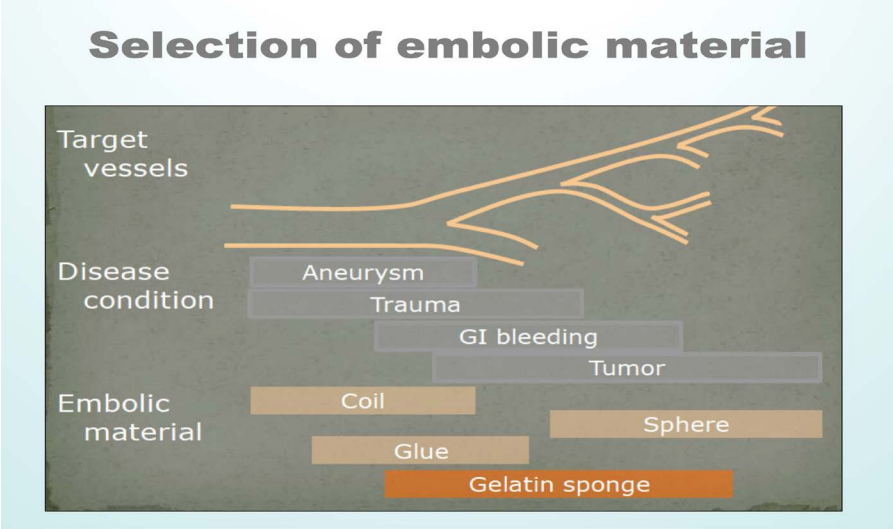


Figure 2

Why Glubran® 2

At this moment in time Glubran®2 (NBCA + Methacryloxy Sulfolane) is the only certified glue for endovascular use in Europe (Fig.4).
The co-monomer allows for better stability and for a spontaneously delayed polymerization time, which makes it less challenging to deploy when compared to Histoacryl® (Fig.5). Another liquid agent is MagicGlue® from Balt, formerly known as Purefill® (Fig.6).
Comparing polymerization time, levels of cytotoxicity and inflammation, and adhesive strength across all available products, Glubran®2 appears to be a perfectly balanced agent in terms of behaviour. It therefore represents a favourable option in many indications.
As costs usually represent a relevant factor, **a great advantage to favoring Glubran®2 is its price**. The price of Ethiodized Oil (Lipiodol®) has been rising consistently over the past 5 years: today, it is about € 250.00 for 10 ml. Since Trufill® comes packaged together with Ethiodized Oil, this may be one

Cyanoacrylates: types and actions

	Methyl (NMCA)	Butyl (NBCA)		Hexyl (NECA)
	Superglue®	NBCA *Histoacryl® Trufill®*	NBCA + CM *Glubran®2*	*MagicGlue®*
CH3 radical	+	++	++	+++
Polymerization time	Very fast	Fast	Intermediate	Low
Cytotoxicity	+++	++	+	+
Inflammation	+++	++	+	+
Adhesive strength	+++	+++	++	+

Used for endovascular purpose

Figure 3

of the reasons for its eccessive cost. A 1 ml vial is about $ 3,000.00, whereas the same amount of Glubran®2 costs about € 100.00. The cost of the mixture may be compared to purchasing a single plug or one detachable microcoil. Onyx® or Squid are about twice the price. Usually, fixing an artery requires 3 to 6 microcoils, whereas a single drop of glue will produce the same results. Another upside is that **Glubran®2 comes in vials of variable capacity (0.25/0.5/1 ml)**. This makes it **quite practical as we do not always need the same amount of product**. While veins require the entire space to be filled, arteries can be occluded by using only a few drops. MagicGlue® from Balt is a "Me too" product in terms of CE marking. This means that no preclinical studies have been made, in fact, the studies from Glubran®2 have been used. The price of this product compares to that of Glubran®2. Glue is used in many fields, not only in interventional radiology but also in surgery. In Europe, it is widely employed in surgical environments, except for France, where the ratio is about 70-30% to interventional radiology.

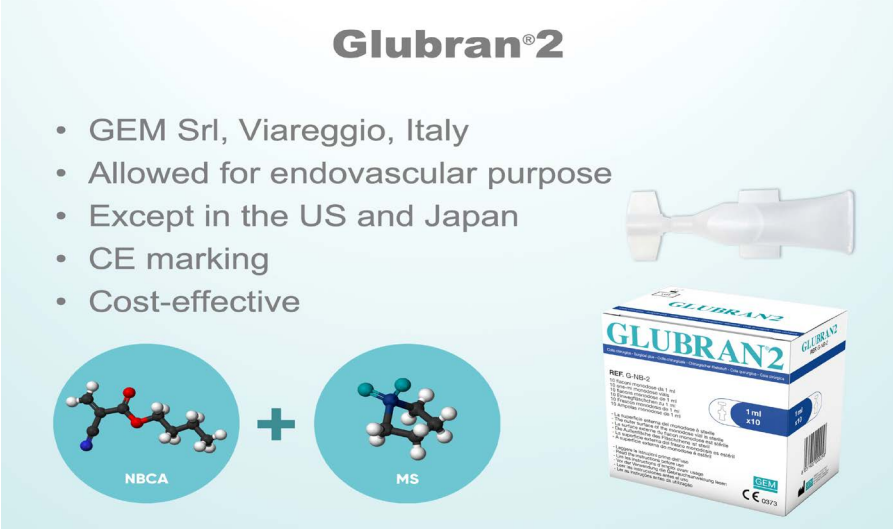


Figure 4

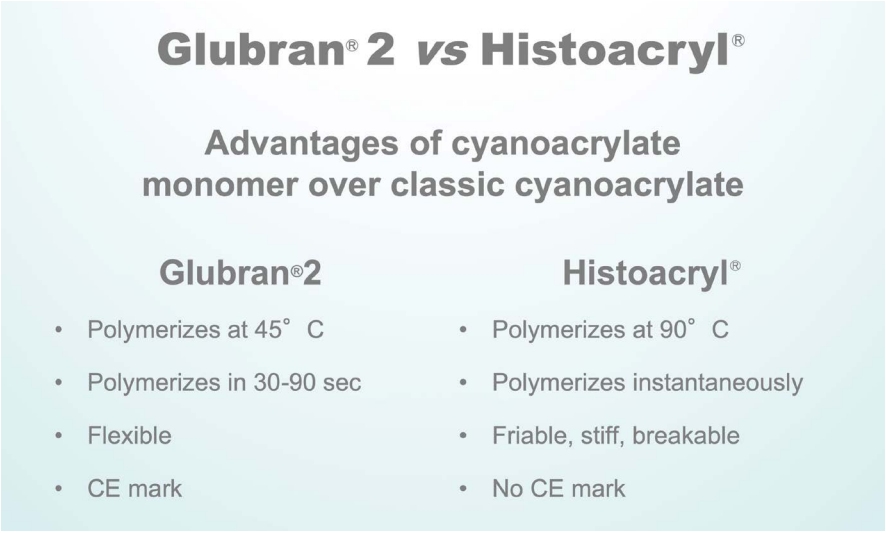


Figure 5

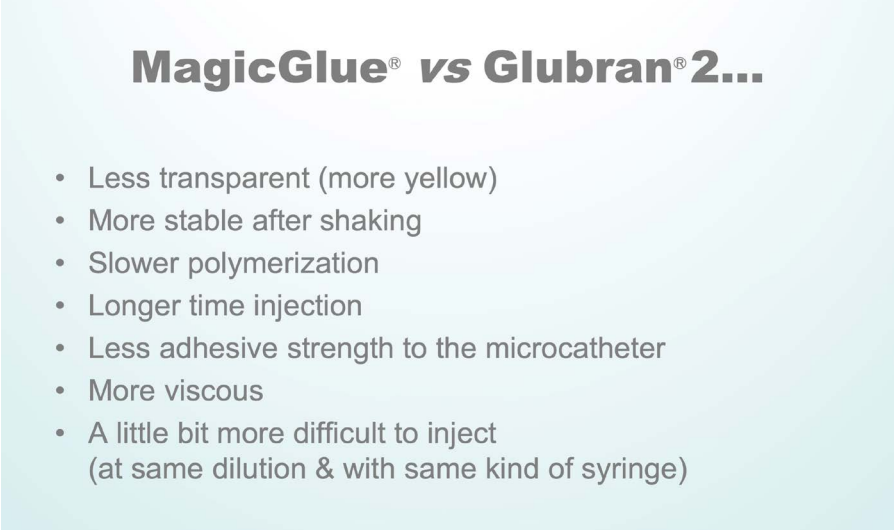


Figure 6

I estimate it is about the opposite in the rest of Europe. MagicGlue® often uses different names depending on the field: in surgery, it is often known as IFABOND, which sounds quite different. Glubran®2, on the other hand, is marketed under the same name in every field. Glubran®2 is transparent, colorless, highly adhesive, and hemostatic (Fig.7).
The fact that the mixture with Ethiodized Oil dissolves polycarbonates might not be of specific interest to interventional radiologists, as we prefer to use different materials, but it is still worth mentioning.
Not only it is an embolic agent, but it is a sclerosant, too, so it can be employed in a variety of indications. It polymerizes in contact with any ion-rich fluid; therefore, it needs to be flushed with a 5% dextrose solution to prevent the blood from refluxing and polymerization from starting inside the catheter. In case of distal embolization such as a tumor, you need to abundantly flush the tumor bed, too, in order to make sure distal embolization is achieved.

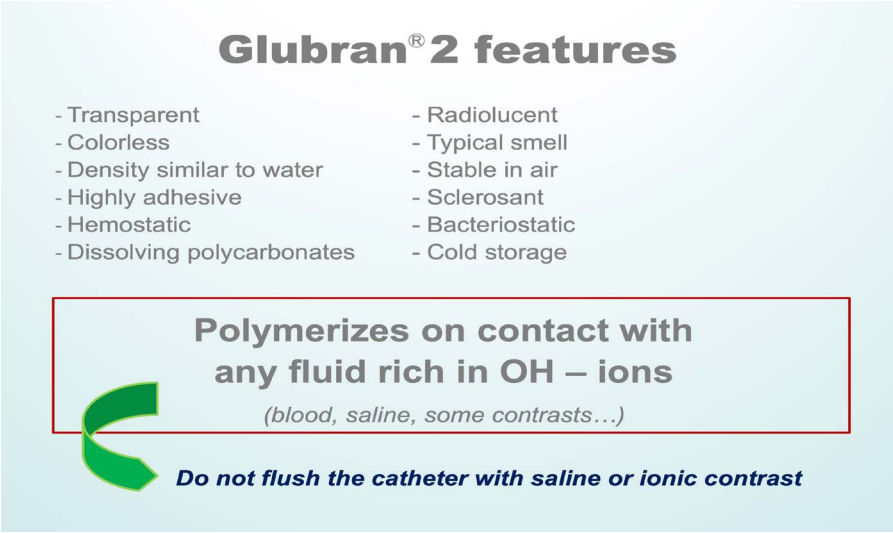


Figure 7

Polymerization of NBCA involves an exothermic reaction that is known to cause pain, even though this mechanism is not clinically obvious. Glubran®2 polymerizes at half the temperature as Histoacryl®, so it causes the patient less pain. Other differences include delayed polymerization, higher flexibility, and official approval. As previously mentioned, the advantages to using Glubran®2 are not limited to cost (Fig.8).

- **A quick embolization also implies less radiations, both for the surgeon and the patient.**
- **This product can be used in a number of indications, with bleeding as perhaps the most suitable.**
- **It is a permanent agent, exceptional when it comes to recanalization. This is not the case with all embolic agents.**
- **The fact that polymerization does not depend on coagulation parameters makes it very interesting in case of bleeding in patients with a coagulation disorder or low levels of platelets.**

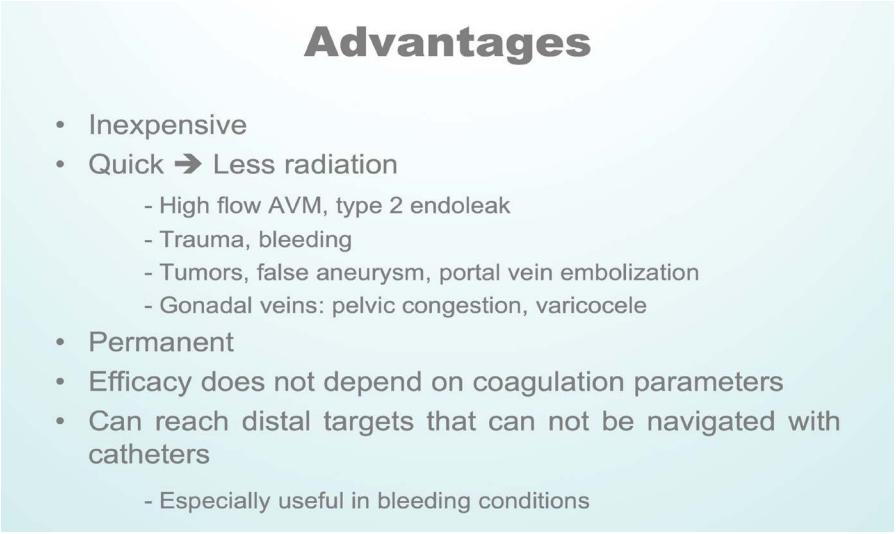


Figure 8

When Glubran® 2 comes into contact with blood, it **never fails to achieve occlusion**. Compared to mechanical agents, this poses a great advantage. In the use of coils, for example, a spontaneous thrombosis needs to be triggered and that can be challenging in patients with coagulation disorders.

- Distal targets are easily accessible even with the smallest microcatheter. In some specific indications, liquids are simply the best option.

When compared to Onyx®, Glubran® 2 is more thrombogenic and quicker to polymerize (Fig.9)[1]. Inflammation rate is also higher. Even though Onyx® may be perceived as safer, as it ensures a more controlled release, in our experience this is not key in any indication. Besides, our concern here is peripheral and visceral application, which is quite different from the neurological area.

As previously mentioned, **Glubran®2 has high adhesive properties, but it still takes a long time for it to stick to the catheter. We have never experienced such an incident**. Onyx®, on the other hand, sometimes needs long breaks between injections, as it often causes immediate reflux.

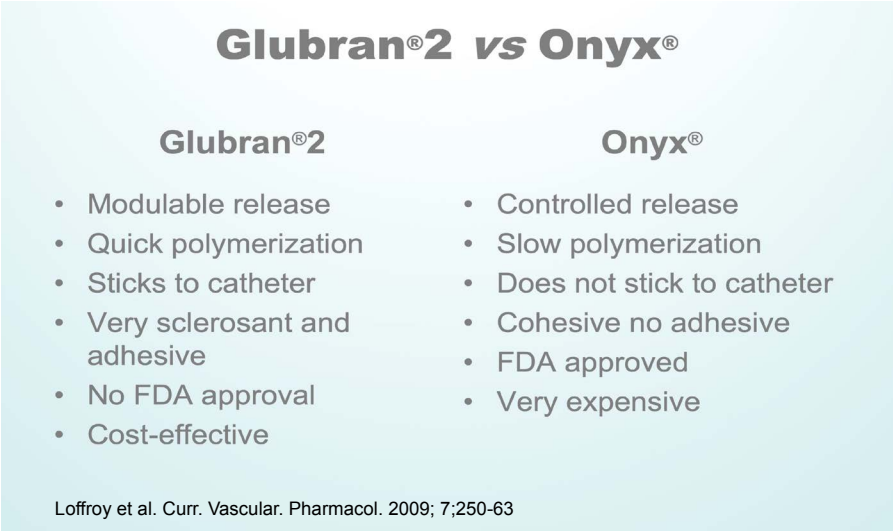


Figure 9

Neuroradiologists may have to wait as long as 45 minutes between injections for a hard cast along the microcatheter to form so that they can push it again into the distal spot. The risk of finding the catheter stuck is quite high in such cases, and this is why there are specific microcatheters with detachable tips, so that the tip can be left in the patient and avoid an undesirable outcome.

Most interventional radiologists see the use of glue as a practice that can lead to multiple complications, chiefly the risk of the catheter sticking to the vessel. During the course of this presentation, some useful advice will be offered towards performing a safe and proper embolization, helping the radiologist to avoid such risk entirely. Generally speaking, **while it may be possible to find the catheter hard to remove, the likelihood of it getting stuck to the point of not being able to remove is non-existent**.

Ischemic risk is also a concern, as many perceive glue as a potentially dangerous agent with high risk of ischemic complications and necrotic lesions. In the past four years, two articles have been published regarding the use of glue in GI bleeding [2,3], showing how cyanoacrylate glue is the most clinically useful embolic agent in treating patients with acute NVIGIB (non-variceal gastrointestinal bleeding), despite the need for a learning curve, especially in cases of coagulopathy.

Despite the bowel being considered as the territory with the highest risk of ischemic complication, we showed that the risk rate is actually lower than with other embolic agents. Microparticles, for example, start from 14 microns in size and, when injected, the risk of ischemic complications is very high. Regardless of the level of dilution, combining Glubran® 2 with Ethiodized Oil makes the mixture highly viscous, which prevents it from reaching the capillaries. A viscous mixture will never become as distal as small microparticles. Non-target embolization caused by reflux is indeed a possibility. Nonetheless, compared to other agents, the upside to employing glue is that it is clearly visible during the procedure. Particles, for instance, are only visible by means of the contrast agent that is added to them.

Although due caution is certainly essential, the endpoint is that cyanoacrylates are easier to handle as they are easier to see.
Besides, as our area of interest is peripheral application, most times a few drops of glue in a non-target vessel will bear no consequences at all, so we can conclude that this kind of complication is not to be considered as such, but rather something we need to be aware of (Fig.10).

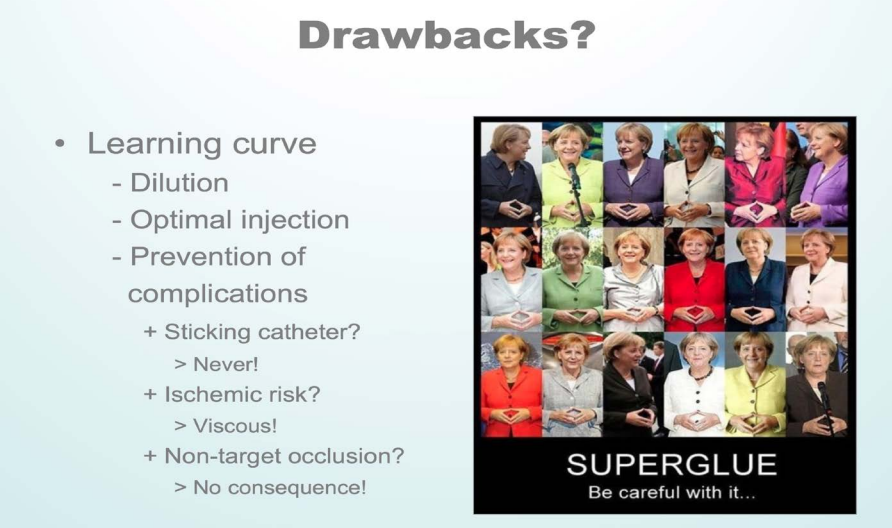


Figure 10

General instructions

Coaxial technique

Using a **coaxial technique** guarantees **better maneuverability** and **additional protection**. **Inserting a microcatheter inside a standard 4 to 5 French catheter is a way to ensure safe and precise movements throughout the entire procedure.** Proceed then with flushing with 5% dextrose solution. Depending on the procedure, the microcatheter will have to be disposed of after use, as it may become too adherent. In case of portal vein embolization or varicocele, for example, the catheter may be used again as long as the next catheterism is not too complex. Going back in a second time will not be necessary after a proper embolization, as only a few drops of glue will ensure a perfect result.

Glubran® 2 + Ethiodized Oil: how to prepare the mixture

Glubran® 2 needs to be combined with Ethiodized Oil not only in order to make it radiopaque but also to be able to modulate the rate of polymerization. Depending on how distal the target is, a different ratio between the products will be needed (Figs.11,12).

In our practice, a 5 ml Luer-Lock syringe and a plastic 3-way stopcock are the standard instruments we use to dilute the glue. Avoid using polycarbonate tools as Ethiodized Oil dissolves this kind of material. A Luer-Lock system not only allows for a firm placement of the syringe but also for easier removal, as the syringe itself can be used to extract the catheter. Glubran®2 and Ethiodized Oil can be mixed by using two separate syringes. In order to make the mixture homogeneous, it is important to proceed slowly, in four or five steps, to avoid polymerization. You can detect such an instance by noticing the mixture turning white. According to dilution, a different gauge may be needed.

Instructions for use (1)

- **Using catheter/microcatheter:**
  - Use the same setup everytime
  - Standard 4 or 5F catheter
  - Microcatheter is mandatory
  - Previous catheter flushing with Glucose or 5% Dextrose
  - Catheter becomes useless after embolization

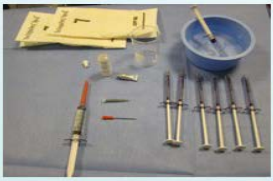


Figure 11

Instructions for use (2)

- **Mixing with Ethiodized Oil:**
  - Makes the mixture radiopaque
  - Modulates the rate of polymerization
  - Plastic 3-way stopcock
  - No polycarbonate luer-locked syringes

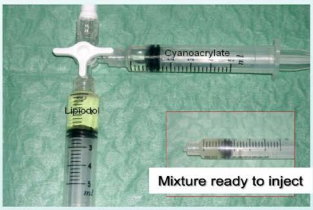


Figure 12

In our experience, a 2.8 Progreat® catheter and a 5 ml syringe offer a good balance between fluidity and resistance. When using a smaller microcatheter such as a 2.0, for instance, the mixture may be quite difficult to inject. In this case, the content of the syringe can be transferred into a smaller one, such as a 3 ml. Using 1 ml syringes is not advisable in our opinion, as the injection may feel too easy and lack the proper resistance.

Embolization technique

Ensure perfect stability of the catheter and perform a detailed angiography prior to the procedure. In order to calculate the volume, concentration, and velocity of the final glue injection, we need to perform several tests using a contrast agent (Fig.13). It is important to understand that the fluidity of these two liquids is not the same, as contrast is quite less viscous. Remember to take this factor into account when you estimate the distribution that the liquid will achieve upon injection.

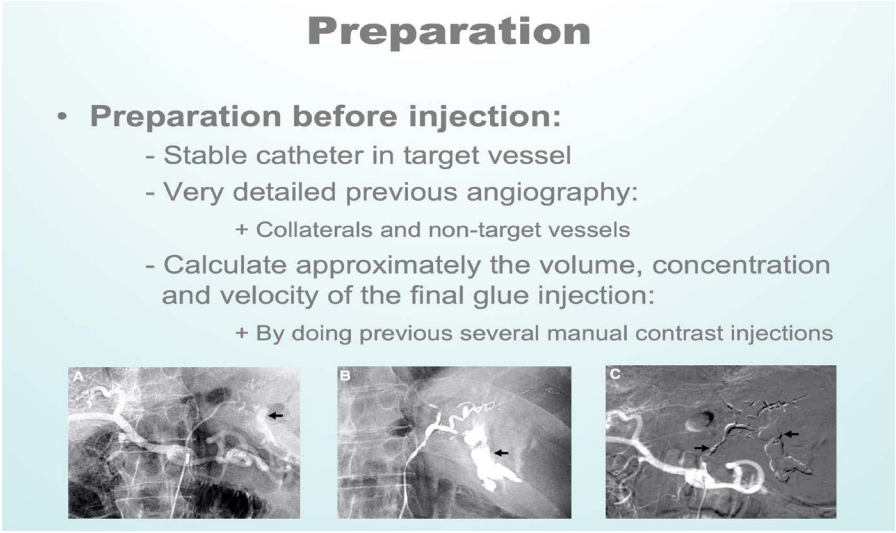


Figure 13

For the same reason, it is strongly advisable to pay attention to the strength we apply to the injections: always make sure you try to perform them in a similar way, so that the distribution of the liquid will be similar when you move on to injecting the mixture.
Figure 13 shows an example of considerable bleeding from the left gastric artery. The patient is hemodynamically stable and the branch can be sacrificed without consequences because of the collaterals. This is a typical embolization and we have a variety of choices to treat such a case. We can use gel foam or coils for example, however, we consider such choices as time consuming, as you may have to use a lot of coils and still not achieve complete occlusion. In this case, two drops of glue will bear great results, quickly, efficiently, and without risk. Conclusively, every time you can sacrifice the bleeding branch, which is most cases, this is undoubtedly the best course of action. Naturally, things would be different with the hypogastric artery or a pelvic trauma, for example.
Provided that we always need to perform a slow and regular injection under strict fluoroscopic guidance, we can use different techniques to achieve proper embolization of our vessel (Figs. 14,15). Firstly, it is worth pointing out that the presence of blood flow does not prevent us from employing glue in our procedure. In fact, it is the opposite. A blood flow means that we can avoid reflux and safely push in the distal spot, as this presentation will show through practical examples. In most cases, though, we will perform a free flow injection.

1) Take a 5 ml syringe of dextrose solution and flush the dead space first, then
2) take another 5 ml syringe filled with the Glubran®2 - Ethiodized Oil mixture and
3) start injecting slowly and continuously. Looking at the tip of the microcatheter, you will eventually see the mixture going distally, followed by a moment of stasis.
4) Your endpoint will be marked by some reflux happening at the tip or of the microcatheter or even a little before that point, and that is when you can stop injecting and
5) proceed to remove the microcatheter with your right hand by the 5 ml syringe itself. The presence of glue in the dead space is of no concern and,

in case of arteries, the 5 F catheter will be patent, which allows for better control through the catheter.

This is not the case with venous embolization when we are in presence of retrograde flow. For varicocele or pelvic congestion syndrome (PCS), when we remove the microcatheter we will likely occlude the 5 F catheter. This is not a problem but something we need to be aware of, since in that case we need to make sure not to push again, as we would be pushing something that is already polymerized and run the risk of migration. Keep in mind that this is indeed a false problem, as pushing again is impossible except with very small syringes. Provided that we perform the injection correctly and remember the difference in behavior between arteries and veins, this one-shot technique is ideal in many situations. Our second option is a multi-shot technique. After flushing the dead space with dextrose solution, we take only a small amount of mixture. As the dead space of a 2.7 microcatheter is about 0.6/0.7, a 0.2 ml is enough. We proceed with slowly injecting glue and dextrose solution in lay-

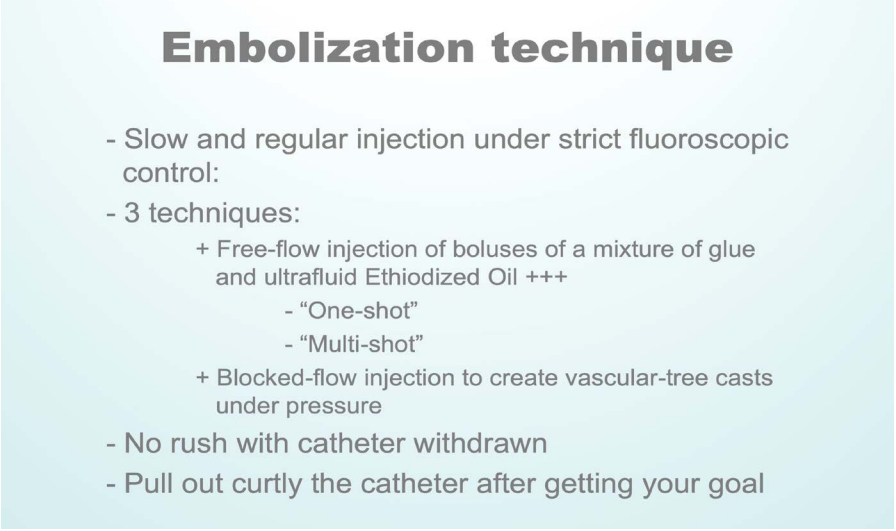


Figure 14

ers, repeating the procedure as many times as needed. This will ensure that the dead space stays patent during the whole procedure. The drawback to this technique is not only that it is time-consuming, but also that the layers will rarely look neatly separated. We can never be sure whether the product at the end of the tip is glue or dextrose, and that is why I personally do not prefer this method, especially considering that maintaining the patency of the microcatheter is, in most cases, not mandatory. Carefully remove the microcatheter, not because it will stick as this is not a real risk, but in case any glue is left on the tip. If so, removing the catheter too quickly may break the glue and cause it to migrate to the distal spot, especially in case of arterial embolization.

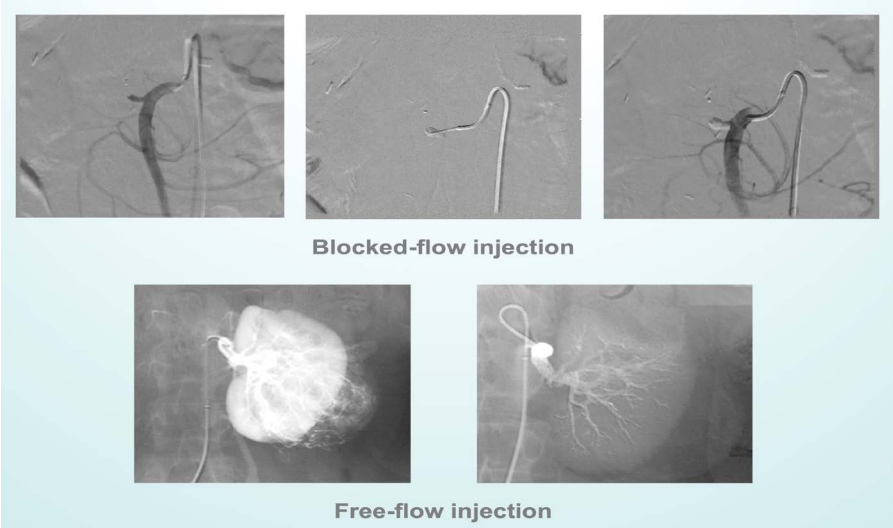


Figure 15

Example

Figure 15 shows a free flow injection performed on a large hypervascular renal tumor. It is not rare to perform an embolization before a total nephrectomy, as this prevents bleeding or transfusions which would complicate the procedure. Reflux does not represent an issue in this case as the kidney can be sacrificed entirely, which makes this an easy embolization for the interventional radiologist. Start by placing a 5 F catheter at the proximal spot and the tip of the microcatheter in the trunk, about 1 cm away. Inject a high diluted mixture, using a 1:5 or 1:6 ratio. Observe the drops going distally and all the branches being reached by the reflux. Wait for stasis and more reflux. When the endpoint is reached, stop injecting and proceed with removing the microcatheter. There are many advantages to using glue. Indeed, this procedure may also be performed using microparticles, however, an additional mechanical agent should be placed at the main trunk, as microparticles alone would not be enough to occlude such a large area. Combining microparticles with coils or plugs means having to deploy two embolic agents, while glues will ensure you can perform both the distal and the proximal embolization by means of one agent only. Looking at the distribution of the liquid, we can observe that only the ostium is left patent for subsequent ligation, while every other part has been homogeneously reached by the glue. The endpoint is much more clearly visible as compared to a procedure performed using microparticles. Time is also a factor to be taken in consideration. Choosing the right size for the microparticles is an empirical process that requires some time. This method is overall rather time-consuming, as it needs to go through many different stages. First, we have to inject the microparticles very slowly, to ensure proper dilution. Then, we have to decide on the right size. We start the injection and wait for stasis, assess patency, add more particles if needed, taking

breaks between injections to allow for the reflux to stop. Glue, on the other hand, is clear, fast, and efficient. A procedure such as this will only take seconds to perform. Particles are perfectly suitable for some indications; however, it is not the same philosophy in terms of injections.
This is a typical free flow injection that is perfectly suitable for training. One thing to keep in mind is that when we embolize such large vessels, we may notice the bolus of glue growing bigger. In this case, do not fear it will not detach. Keep pushing and apply pressure to make sure it detaches and goes distally. As long as we do not have reflux, we can safely keep injecting the mixture. Once the glue has gone distally, wait for reflux and safely remove the microcatheter. You do not need to wait before doing so.
Figure 15 shows a pseudoaneurysm in the main trunk of the superior mesenteric artery. Most people would probably use a covered stent in this case; however, glue is a favorable alternative that will save the patient form having to take antiplatelet medications or risking long-term in-stent restenosis (ISR). We can use a very low dilution such as 1:0.5, just to make the mixture radiopaque while ensuring fast polymerization. Place the tip of the microcatheter at the back of the false aneurysm and inject very slowly to form a cast. The aneurysm will be filled and nothing will be left in the main trunk. Make sure you refrain from removing the microcatheter too soon and wait about 5 minutes for the polymerization to complete. Retracting the catheter too soon may result in the cast of glue being pulled back and migrating to the main trunk. There is no risk for a hydrophilic microcatheter to stick, especially considering we have the 5 F as a support.

Polymerization

Polymerization starts one or two seconds after the mixture comes into contact with blood, however, depending on the patient, we have one or more minutes before it ends. In case of distal embolization, after flushing the dead space we also abundantly flush the vascular bed to regulate the speed of the polymerization process (Fig.16). In a prostatic artery embolization, for example, we flush the gland and the distal bed with 5 or 10 ml of dextrose solution to leave the glue enough time to go distally. The ratio of our dilution also affects polymerization time. A more diluted mixture will take longer to complete the process (Figs. 17,18).
In most cases we use a 1:3 ratio. Almost any ratio will work with arteries.

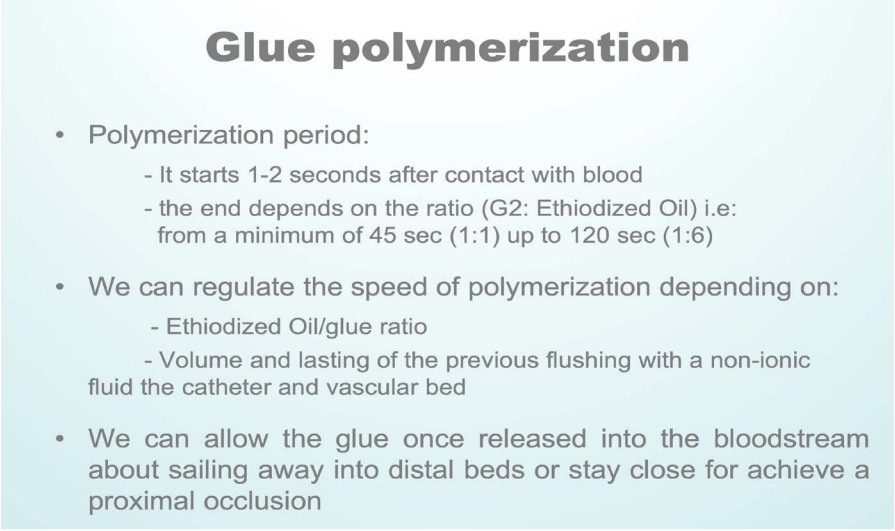
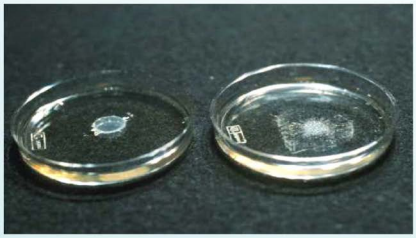


Figure 16

Polymerization time

NBCA-Ethiodized Oil mixture
dropped on plasma



1:1 mixture
(50% NBCA)

1:4 mixture
(20% NBCA)

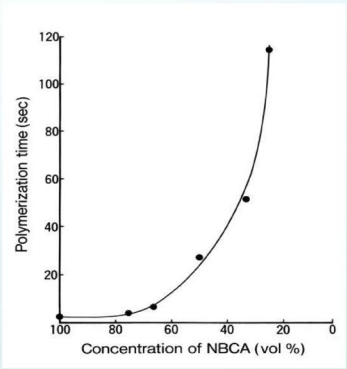


Figure 17

Choosing glue dilution

NBCA-Ethiodized Oil ratio

	Low dilution (1:1 – 1:3)	High dilution (1:4 – 1:9)
Catheter position	Close to lesion	Away from lesion
Catheter tip	Wedged	Free
Injection manner	Continuous column	Drop by drop
Flow speed	Fast	Slow
Occlusion	Segmental	Peripheral
Application	Shunt	Organ, end artery

Figure 18

For veins, a pelvic congestion syndrome (PCS) or a varicocele, use a 1:1 low dilution. In case of reflux, we need to avoid migration at renal vein level. When we use a highly diluted mixture, we cannot intervene on the reflux as we first need to wait for the polymerization to complete. With a 1:1 ratio, polymerization starts immediately and there is no time for the glue to migrate, even in case of reflux. In case of distal embolization, for example with tumors, use a high dilution of 1:5 1:6. Also, when the tip of the microcatheter is far from the bleeding site and you need to reach the distal spot, use a higher dilution.

Dilution ratios per indication

What follows is a short list of indications with the respective dilution ratio. In clinical practice (Fig.19):

- 1:1 for varicocele
- 1:3 for 80-90% of cases
  - Peripheral bleeding
  - Pseudoaneurysms
  - GI bleeding
- 1:5 for peripheral AVMs
- 1:8 for portal vein embolization & PAE

The highest dilution is used in case of low flow, such as in procedures involv-

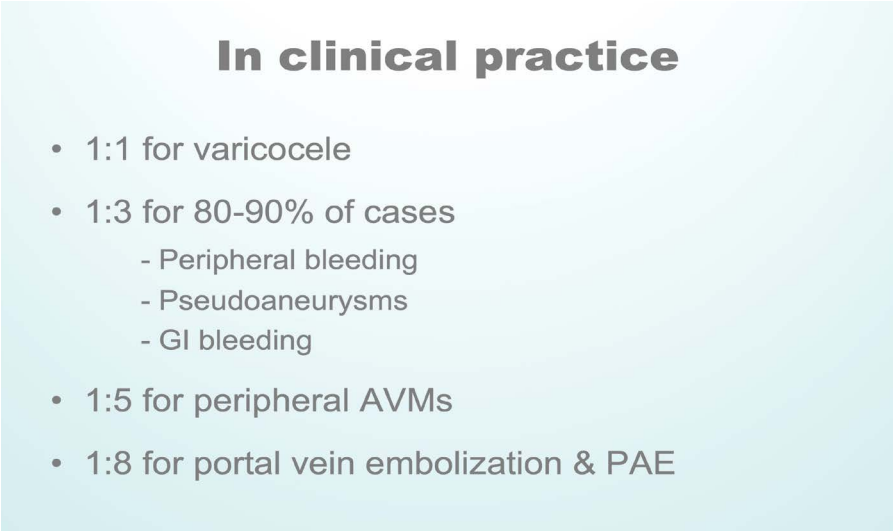


Figure 19

ing the portal vein system. A high dilution such a 1:8 ensures you can achieve a distal embolization.
At this moment in time, it appears that a plateau is reached at a ratio of 1:8 - 1:10. Beyond this point, while there would be no noticeable improvement in performance, the risk is that an excessively diluted mixture would result in poor adherence to the wall and the vessels, and may cause migration of the glue at a later time, when the patient is standing.
Now, we are going to show some examples of indications where glues have proved to be powerful allies.

Clinical applications

Arterial approach

The following are the clinical applications of the Glubran®2-Ethiodized Oil mixture [4] (Fig.20):

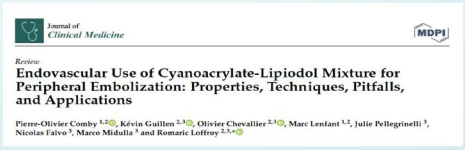
- Arteriovenous malformations (AVM)
- Acute arterial & venous bleeding
- Hypervascular tumors (primitive/metastasis)
- Portal vein embolization
- Endoleaks
- Varicocele / pelvic congestion syndrome
- Hypersplenism
- Prostatic artery embolization (PAE)
- Non-vascular purpose:
  - Needle track embolization
  - Enterocutaneous leaks
  - Biliary tract

Buttock AVM

In this first example we have a painful buttock AVM. The MR image shows it is very superficial (Fig.20AF). We first attempted an arterial approach and soon realized it was impossible to reach the nidus that way. We proceeded then by puncturing the nidus by the means of a 21 G Chiba needle and injected a 1:4 mixture of Glubran®2 and Ethiodized Oil. In a case such as this, extra caution is required to avoid venous drainage, however, when you first inject contrast to assess the flow, remember this liquid is rather less viscous than a 1:4 mixture of glue, and that makes it more likely to reach collaterals. Inject the glue slowly but do not worry about reaching as far as the contrast.

Clinical applications

- AVM
- Acute arterial & venous bleeding
- Hypervascular tumors (primitive/metastasis)
- Portal vein embolization
- Endoleaks
- Varicocele / pelvic congestion syndrome
- Hypersplenism
- PAE
- Non-vascular purpose:
  - Needle track embolization
  - Enterocutaneous leaks
  - Biliary tract


Journal of Clinical Medicine

MDPI

Review

Endovascular Use of Cyanoacrylate-Lipiodol Mixture for Peripheral Embolization: Properties, Techniques, Pitfalls, and Applications

Pierre-Olivier Comby [1,2], Kévin Guillen [2,3], Olivier Chevallier [2,3], Marc Lenfant [1,2], Julie Pellegrinelli [3], Nicolas Falvo [3], Marco Midulla [3] and Romaric Loffroy [2,3,*]

Figure 20

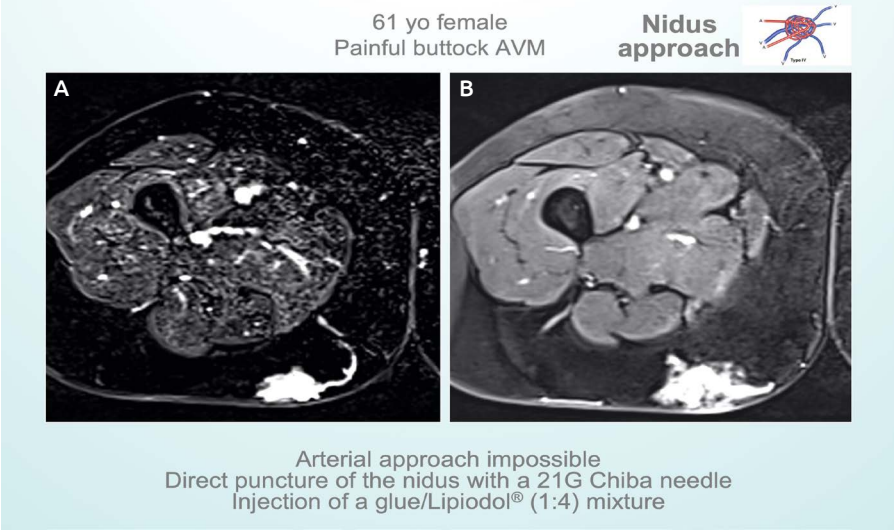


Figure 21 AB - 61 yo female - Painful buttock AVM - Nidus approach

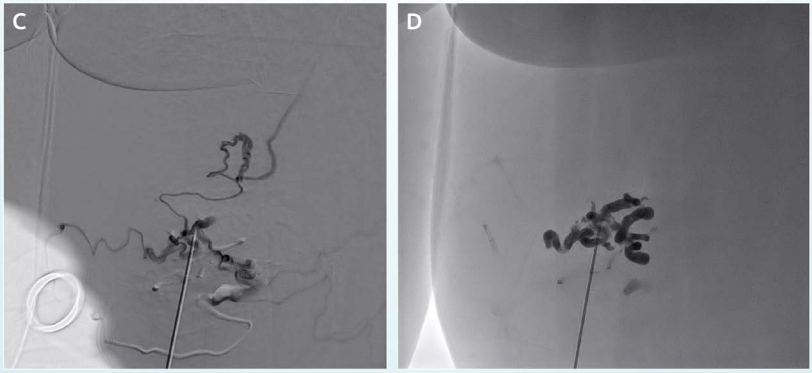


Figure 21 CD

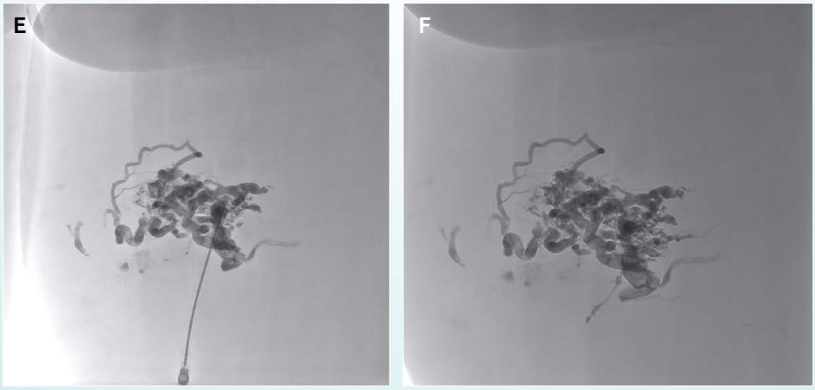


Figure 21 EF

In case of venous drainage in arms or legs, you can apply compression to stop the process. Keep injecting until you completely fill the nidus and reach your endpoint. Even though Onyx® might seem a good choice here, in case of very superficial AVMs it can be overly painful for the patient and sometimes leave marks on the skin. Glue is an easy and safe alternative.

Uterine AVM

A bleeding uterine AVM post-abortion with pseudoaneurysm and venous drainage (Fig.22AI). Using microparticles in this case would pose a serious risk of migration, whereas employing gel foam might result in an incomplete embolization. Notice how the microcatheter advances a long way, forming several loops. Nonetheless, the tip is quite far from the distal spot. Even in such a case, by using a 1:5 mixture we can achieve complete occlusion, as the glue travels distally enough to reach the spot. While copolymers are useful in many indications, they cause immediate reflux, which forces us to wait for

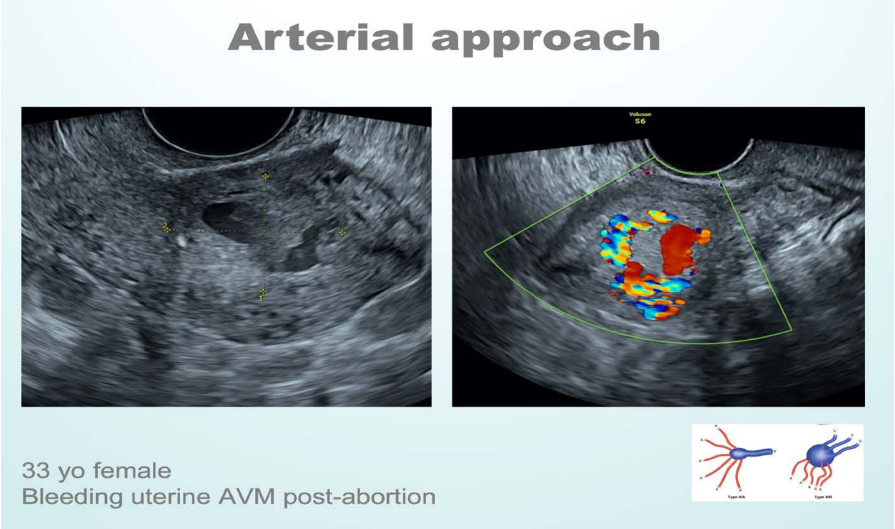


Figure 22 AB - 33 yo female - Bleeding uterine AVM post-abortion

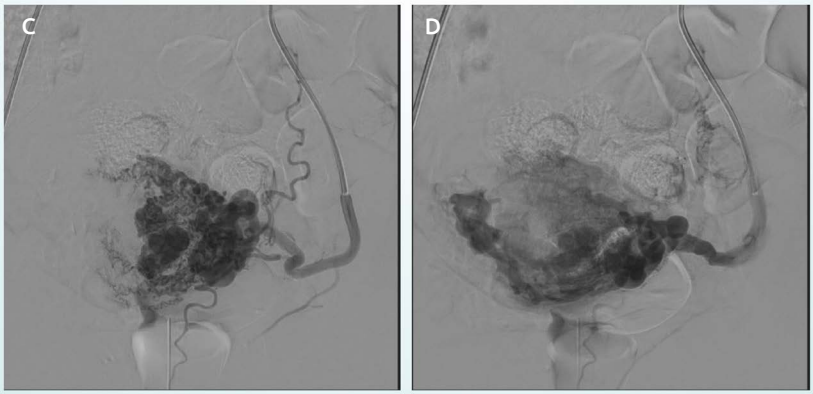


Figure 22 - C: initial angio arterial, D: initial angio venous

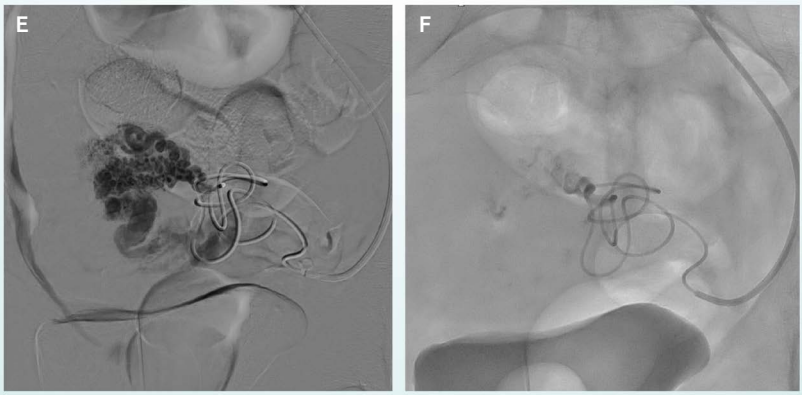


Figure 22 - E: first feeder before embolization, F: first feeder after embolization

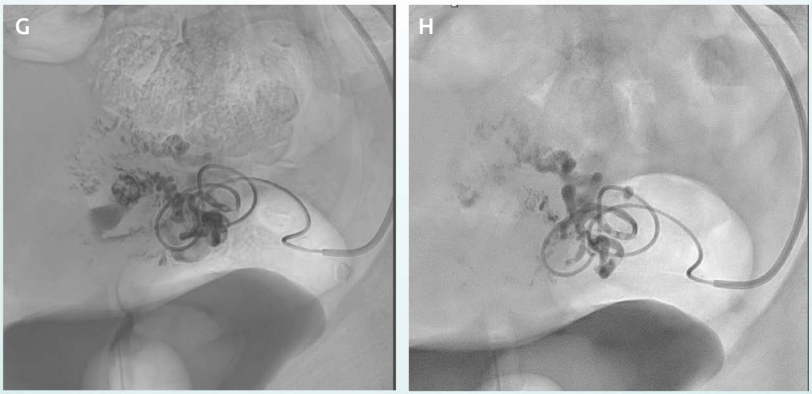


Figure 22 - G: second feeder before embolization, H: second feeder after embolization

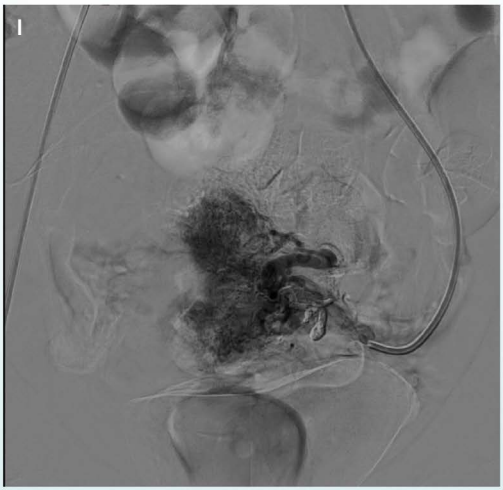


Figure 22 - I: final control

the cast along the microcatheter to harden, in order to be able to push again. Besides, when the tip is too far, Onyx® or Squid simply cannot be pushed distally enough. Glue here poses no risks. Reflux on the catheter is a non-issue, as it will not prevent safe removal. Migration to capillaries is not common in case of AVMs such as, for example, a renal tumor. The case would be different with direct connections, for example a fistula. However, should you feel doubtful, you have the possibility of doing a test with Ethiodized Oil alone first. The final result shows patency of the main uterine artery with both branches correctly embolized. Microcatheter withdrawal can be performed while injecting, however this is not compulsory. In case of big arteries, we can place the tip in the main artery and use a highly diluted mixture. In other cases, if we have reasons to be selective and maintain the rest of the tumor bed patent, we can place the tip at the furthest point and inject while retracting. These are just two different options. Here, the several loops the microcatheter forms tell us we are very distal, however, even in case of reflux along the microcatheter, removing it will not be a problem. If we feel we are at the endpoint and we need to leave the microcatheter in place for 30 seconds or so, there is no reason to worry, we can just proceed with the removal.

Cardiac hyperflow related dyspnea

Here is a case of cardiac hyperflow-related dyspnea (Figs.23-25) with a huge malformation in the inferior mesenteric artery. It is a typical AVM with a large dilation of the venous drainage. We started with a balloon-assisted embolization with Onyx® to slow down the flow, however, we soon realized the process was taking too long, and we agreed to use glue instead. This is due to the presence of many branches, which are easier and quicker to catheterize with glue. Thanks to the viscosity of the mixture, we have no passage to capillaries. The final result is rather good. The advantages to using glue in a case such as this are clearly visible. Employing mechanical agents is not an option here, as our goal is to reach the nidus. Big microparticles pose a high risk of recruitment of collaterals in such a long procedure. Glue, on the other

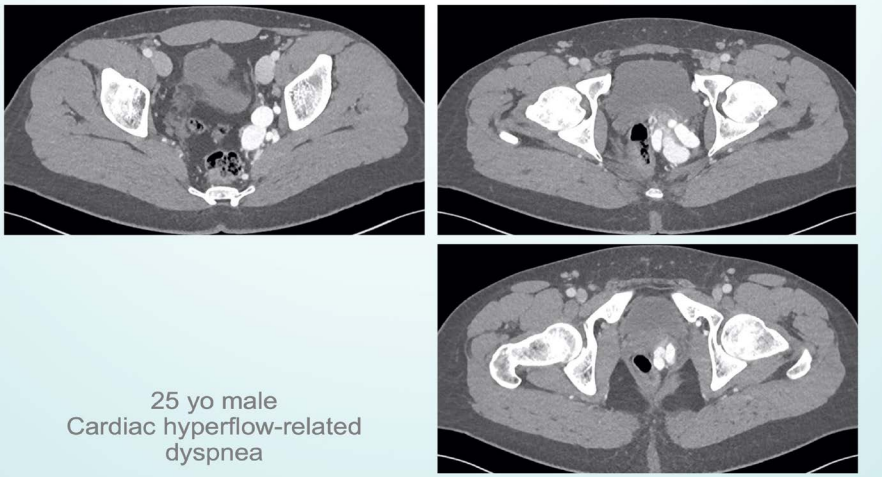


Figure 23 - 25 yo male - Cardiac hyperflow-related dyspnea

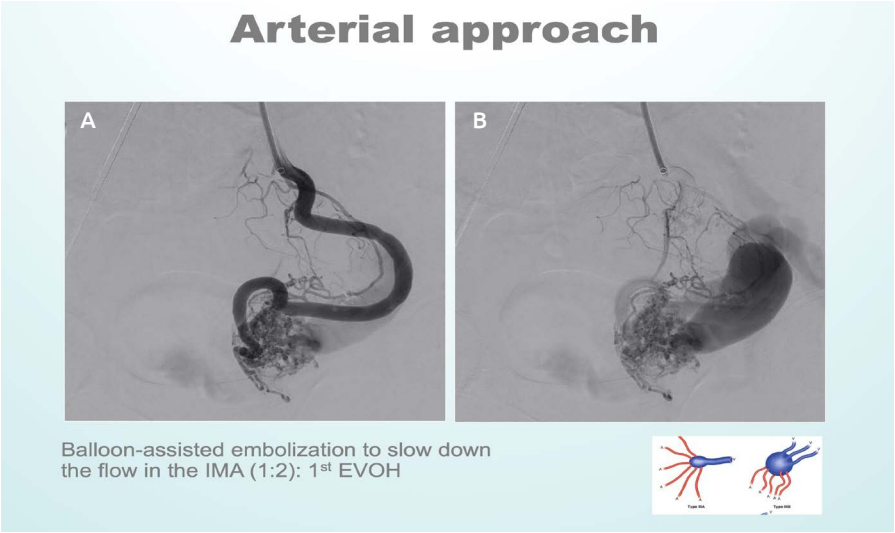


Figure 24 AB

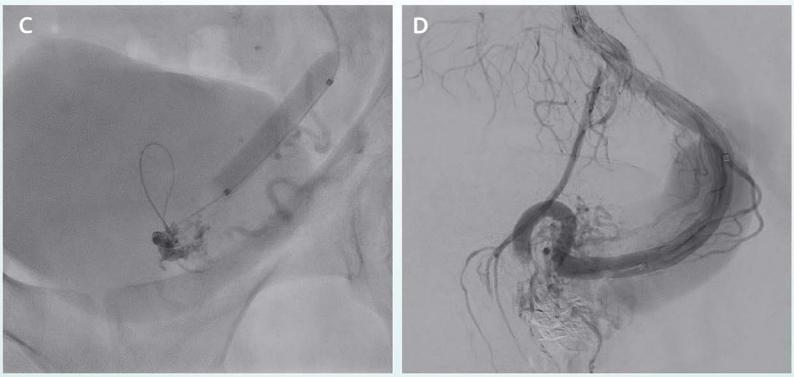


Figure 24 CD

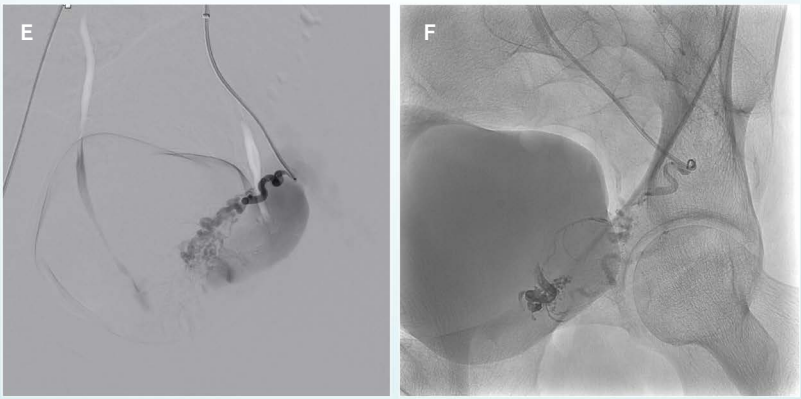


Figure 24 EF

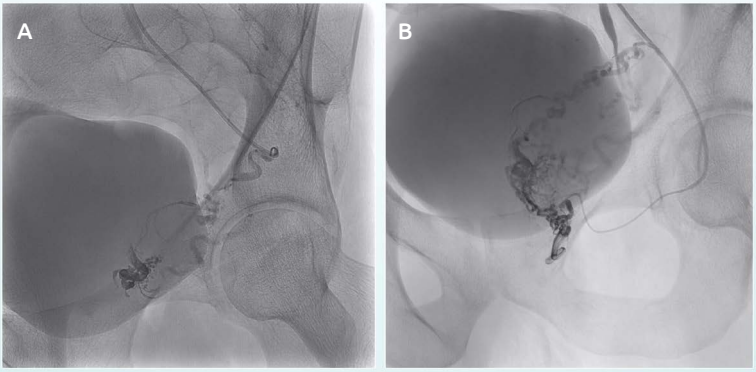


Figure 25 AB

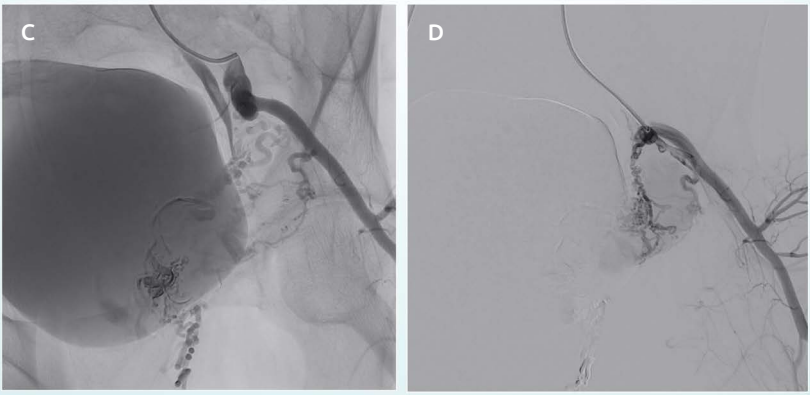


Figure 25 CD

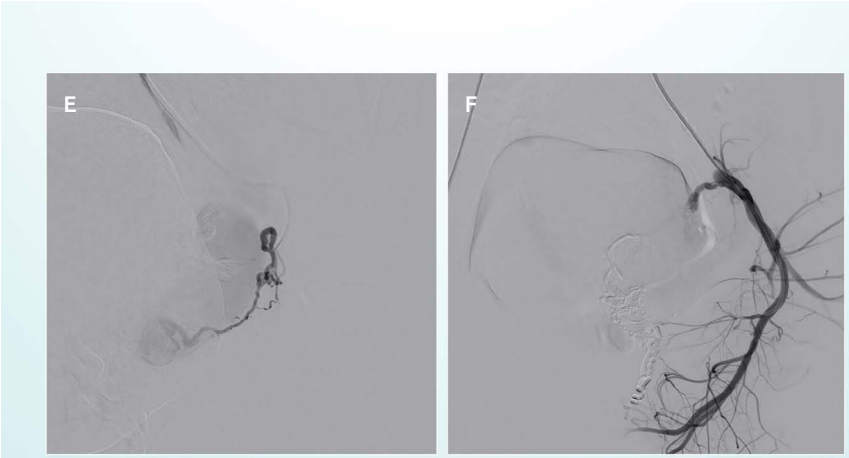


Figure 25 EF

hand, is fast and risk-free. At CT scan we can observe thrombosis of the venous dilation and the distribution of the glue with no passage.

Endoleak type II

Here is a type 2 endoleak where arterial approach (Fig.26), though preferable in my opinion, proved impossible. In order to perform a percutaneous approach, we first insert a metal needle in which we place the microcatheter, to prevent high pressure reflux from pushing it out. We use an ordinary kit for biopsy or nephrectomy and insert a 17 G needle under fluoroscopic guidance at CT scan. We then place a valve at the proximal port of the needle to lock the 2.4 F microcatheter in place. This method will reduce the pressure of the reflux and leave us enough time to inject a 1:4 mixture with no risk of occluding the dead space and trigger early polymerization. While Onyx® might appear as a good indication in this case, we need to take into account the large number of artifacts, even though the amount of tantalum has been

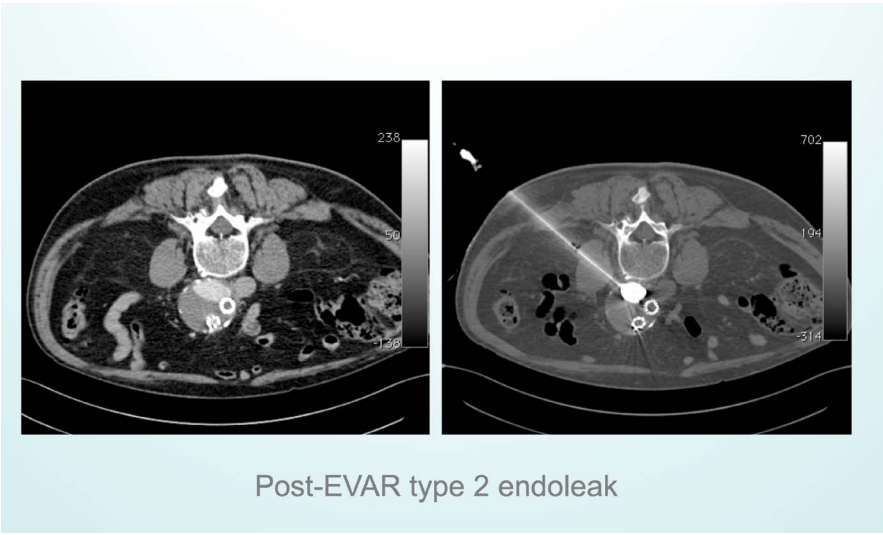


Figure 26 - Post-EVAR type 2 endoleak

recently reduced in both Squid and Onyx®. At CT scan, we can observe a low quantity of artifacts after the procedure with Glubran®2 / Ethiodized Oil.
Figure 27 shows an example of a type 2 endoleak A and B involving the inferior mesenteric artery, which is patent. In such cases, we usually start by accessing Riolan's arcade and then close the artery with coils, as the reflux would make deploying liquids challenging, if not impossible. As we can observe, the catheterism through the iliolumbar artery is quite complicated and we have extravasation, which does not allow to place the tip too distally. Nonetheless, this is not an issue. Just keep checking for dangerous collaterals and start injecting a 1:5/1:6 ratio mixture to reach the other side through reflux. Ensure both lumbar arteries are blocked, as well as the main nidus. Injection by direct puncture of the sack under CT guidance is not advisable, in our opinion, as triggering reflux in the lumbar arteries is not always an attainable goal and this may result in an incomplete embolization. We had a case in which we tried a transabdominal approach and injected the mixture

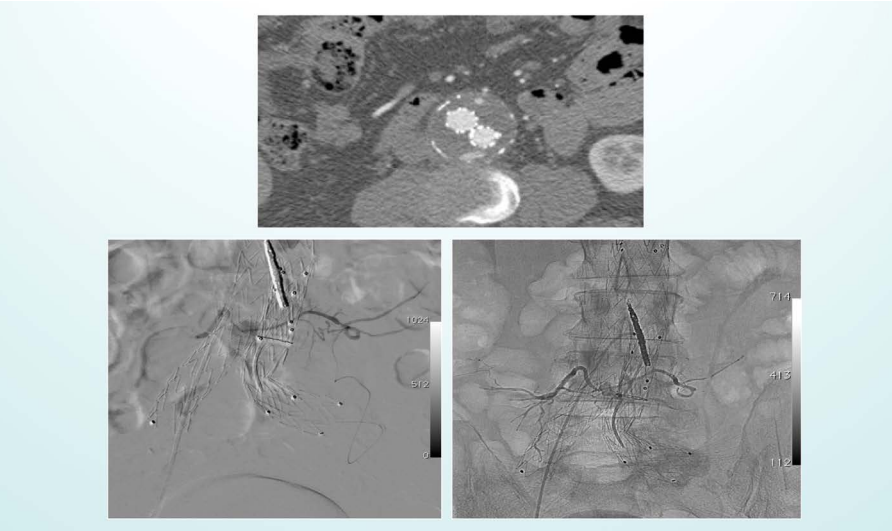


Figure 27 - Type 2 endoleak A and B

by direct puncture of the sack. We got reflux from a patent inferior mesenteric artery, which made us believe it was thrombosed but in fact it was not. Some glue migrated into the sigmoid branches. Fortunately, this brought no consequences for the patient, who was asymptomatic, however, the complications deriving by a cast of glue blocking the main trunk of the mesenteric artery can be disastrous. This is why it is crucial to check that the inferior mesenteric artery is occluded before injecting the mixture in the sack.
In a percutaneous approach, the dilution depends on the size of the artery. If it is big, choose a 1:4/1:5 ratio with a 3 ml syringe and a 2.4 F catheter. There is no need to keep injecting while retracting the catheter. You might need to prepare multiple syringes filled with mixture to ensure you have enough liquid to complete it. A fluoroscopy prior to the procedure may help to assess the outcome in advance. As previously mentioned, reflux in the main lumbar artery is not always attainable, so ensure the injection is performed very slowly in order to be able to correctly detect the endpoint.

The problem with injecting in the sack is that the liquid we are injecting causes engrossment and that is why it is difficult to understand when the endpoint has been reached. The same will happen with copolymers. We usually inject 5 or 6 ml of Onyx® or Glubran®2, however, at times this quantity will not be enough.

False aneurysm

This is a false aneurysm of the hepatic artery (Fig.28) that we attempted to treat with a covered stent that was not well deployed. We found it impossible to retrieve the stent and still detect patency, which led us to successfully attempt a percutaneous approach with direct injection of glue in the pseudoaneurysm.

Angiomyolipoma

Benign tumors such as an angiomyolipoma are good example of glue embo-

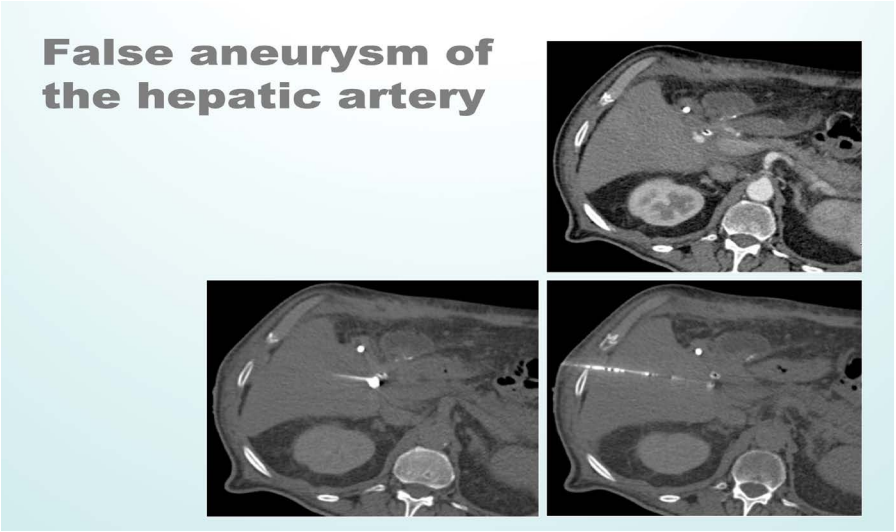


Figure 28 - False aneurysm of the hepatic artery

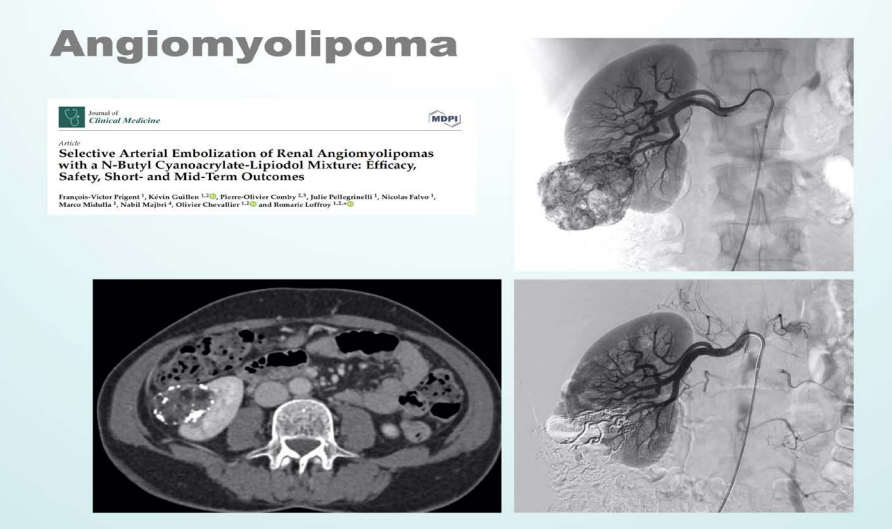


Figure 29 - Angiomyolipoma 1

lization (Fig.29). Here we have two main arteries for which we used a 1:5/1:6 ratio. We abundantly flushed using about 10 ml of dextrose solution and observed the drops of glue going distally until we got reflux. At that point, we stopped injecting and removed the microcatheter. In this kind of procedure, you have the possibility to check your progress step by step, which makes the procedure fast and neat, when compared to using microparticles. The same microcatheter may be reused after careful flushing with dextrose solution. Observe the even distribution of the agent. We recently published a paper on this procedure [5]. Figure 30 shows another example of a typical angiomyolipoma with a large hematoma and multiple aneurysms.
Having a single branch to intervene on makes this the perfect embolization. Use a 1:6 ratio and flush abundantly. Watch the glue go distally, wait for stasis and then for reflux. Stop injecting and retrieve the microcatheter. The whole process is very fast and simple when performed with glue. Microparticles are not a comparable alternative, as the same procedure would take

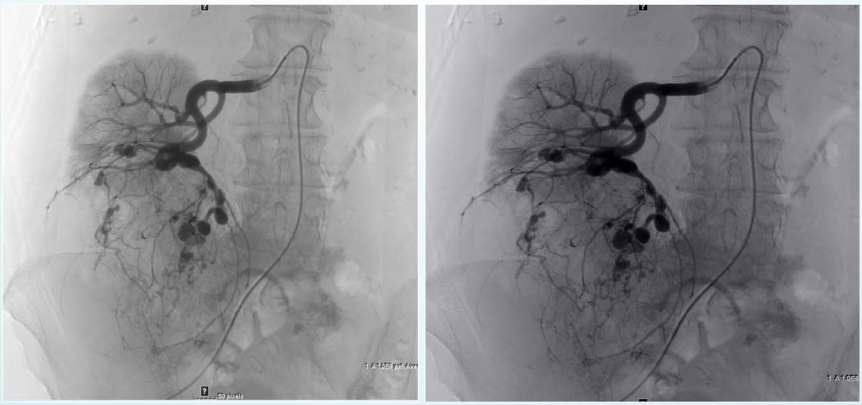


Figure 30 - Angiomyolipoma 2

about two hours to complete. Choosing the right size for the microparticles is a time-consuming decision as it is empirical and may need different tests.
Besides, microparticles alone would not be enough to occlude the aneurysm, some other agent would have to be added at the proximal port or coils would have to be deployed after catheterizing each branch. Glue guarantees perfect results and can be used for both the distal and proximal embolization. Do not hesitate to flush abundantly using between 5 and 10 ml of dextrose solution.
Keep in mind that the highest the dilution, the biggest the quantity of mixture at our disposal.
When we employ a 1:1 ratio, the total amount of liquid amounts to 2 ml, which might not be enough for veins, PCS, or large varices in women. In those cases, remember to prepare in advance a few extra syringes already filled with mixture, as 2 ml would not be enough to completely occlude the pelvic reservoir and the main left ovarian vein.

Kidney pseudoaneurysm

Here we have a pseudoaneurysm in the kidney due to complications occurred after a partial nephrectomy (Fig.31). Placing the tip of the microcatheter at the bleeding site will allow to successfully conclude the procedure with as little as two drops of glue.
Choose a 1:3 dilution ratio, but keep in mind that these conditions allow for any ratio to work. Using coils might seem a safer choice here, however, the risk with coils is for the embolization to be more proximal than expected and to have to sacrifice a lot of collaterals to occlude the main branch. Glue represents a faster and safer choice, provided that we pay the proper attention.

Humeral bone metastasis

An example of a hypervascular humeral bone metastasis from kidney tumor (Fig.32). It is very similar to a high flow AVM and thus presents serious risk of venous passage, which discourages the use of microparticles.

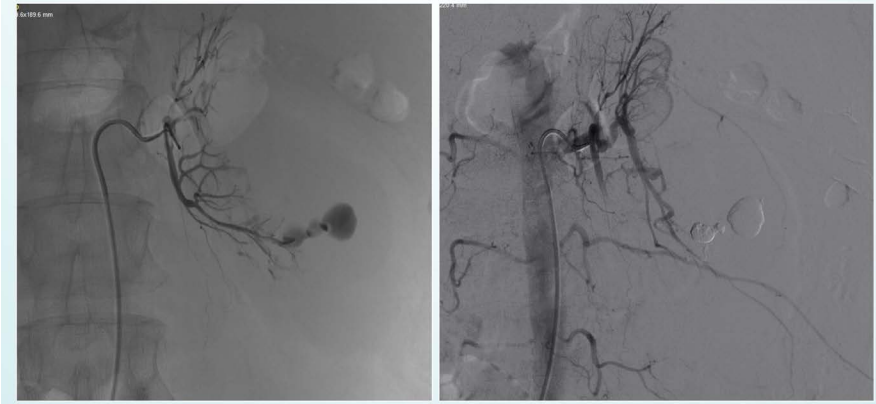


Figure 31 - Pseudoaneurism of the kidney

We catheterized three branches using a 1:1 dilution ratio. Performing a test using Ethiodized Oil alone is a safe way to assess transvenous passage before the actual procedure. The cast of Glubran®2 in the different branches is clearly visible and the final result is extremely good. Using big microparticles in such an indication may appear as a valid option, however, time always represent an important factor to take into consideration. The embolization will take longer to complete, and it will very likely lead to recruitment of collaterals. Glue, on the other hand, will allow you to promptly cut the flow.

Tibial bone metastasis

Another case of hypervascular metastasis from kidney tumor prior to surgery for which we used a 1:5 dilution ratio (Fig.33). We can see the cast of glue perfectly occluding the two main branches of the popliteal artery. Once again, the procedure was completed in a remarkably short time.
A randomized study from Portugal [6] has recently compared cyanoacrylates

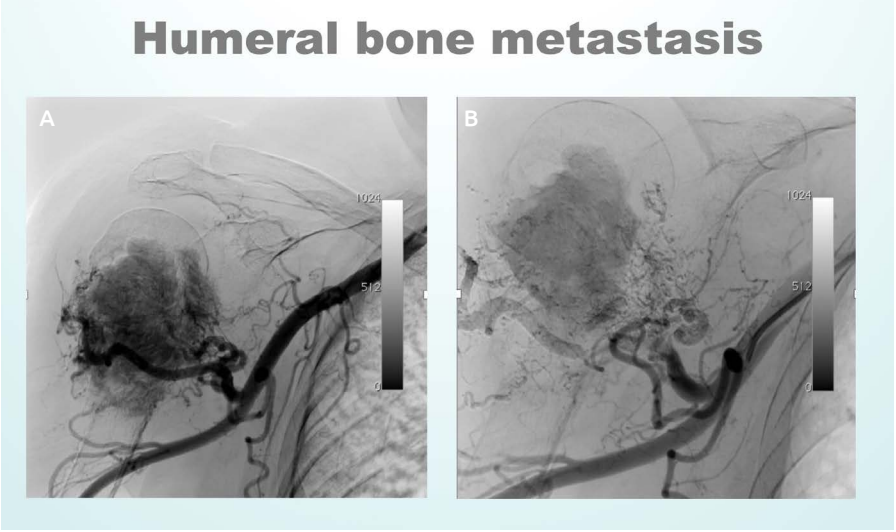


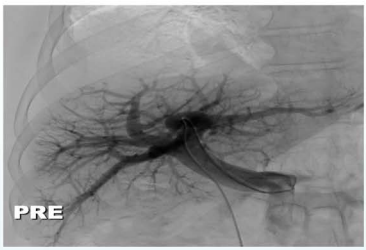
Figure 32 - Humeral bone metastasis: (A) before embolization; (B) after embolization.

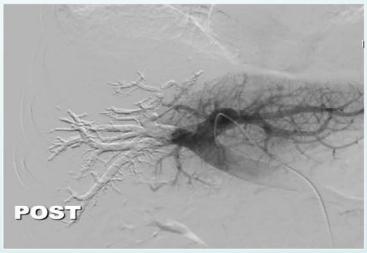
Figure 33 - Tibial bone metastasis: (A) before embolization; (B) after embolization.

with particles plus coils and concluded as follows: "*Portal vein embolization with N-butyl-cyanoacrylate plus iodized oil produced greater and faster liver growth as seen at CT in participants with liver cancer, compared with portal vein embolization with polyvinyl alcohol particles plus coils, allowing for earlier surgical intervention*" (Figs.34,35).

Previous studies also testified to the safety of using NBCA in portal vein embolization, as concluded by a 2018 systematic review and meta-analysis, which stated that: "***PVE utilizing NBCA*** *to induce hypertrophy of the FLR prior to contralateral lobe resection in the setting of hepatic malignancy* ***is safe and effective***" [7]. Although particles and coils are widely used in this kind of procedure, not only are they extremely time-consuming, but the results are hardly comparable.

We used a standard contralateral approach from the right side. We first inserted a sheath, then a 5 F catheter in the main branch, and finally a microcatheter, quite distally. Using a 1:8 dilution we started to inject the mixture





group (*P* = .27). Conclusion Portal vein embolization with *N*-butyl-cyanoacrylate plus iodized oil produced greater and faster liver growth as seen at CT in participants with liver cancer, compared with portal vein embolization with polyvinyl alcohol particles plus coils, allowing for earlier surgical intervention. © RSNA, 2021 *Online supplemental material is available for this article.* See also the

Randomized Controlled Trial > Radiology. 2021 Jun;299(3):715-724.
doi: 10.1148/radiol.2021204055. Epub 2021 Apr 6.

BestFLR Trial: Liver Regeneration at CT before Major Hepatectomies for Liver Cancer–A Randomized Controlled Trial Comparing Portal Vein Embolization with *N*-Butyl-Cyanoacrylate Plus Iodized Oil versus Polyvinyl Alcohol Particles Plus Coils

José Hugo Mendes Luz [1], Filipe Veloso Gomes [1], Nuno Vasco Costa [1], Inês Vasco [1], Elia Coimbra [1], Paula Mendes Luz [1], Hugo Pinto Marques [1], João Santos Coelho [1], Raquel Maria Alexandre Mega [1], Vasco Nuno Torres Vouga Ribeiro [1], Jorge Tiago Rodrigues da Costa Lamelas [1], Maria Mafalda de Sampaio Nunes E Sobral [1], Silvia Raquel Gomes da Silva [1], Ana Sofia de Teixeira Carrelha [1], Susana Cristina Cardoso Rodrigues [1], António Augusto Ferreira Pinto de Figueiredo [1], Margarida Varela Santos [1], Tiago Bilhim [1]

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https://doi.org/10.1007/s00270-018-1964-6

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REVIEW

Portal Vein Embolization Utilizing *N*-Butyl Cyanoacrylate for Contralateral Lobe Hypertrophy Prior to Liver Resection: A Systematic Review and Meta-Analysis

Ethan Wajswol[1] · Tarek Jazmati[2] · Sohail Contractor[2] · Abhishek Kumar[2]

Figure 34 - Portal vein embolization

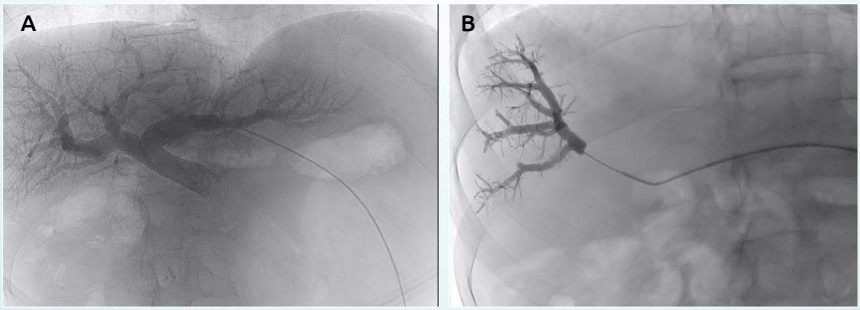


Figure 35 AB - Portal vein embolization.

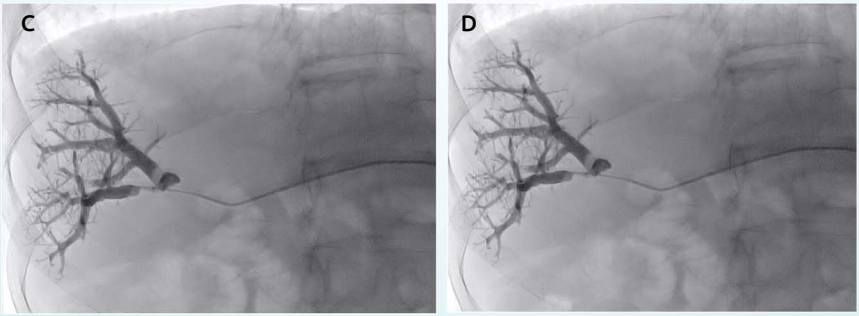


Figure 35 CD

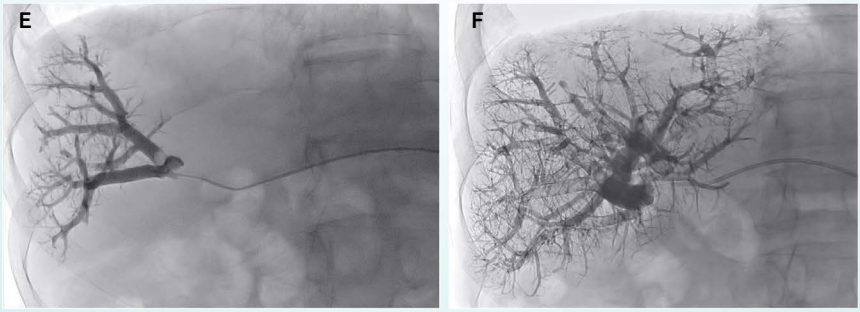


Figure 35 EF

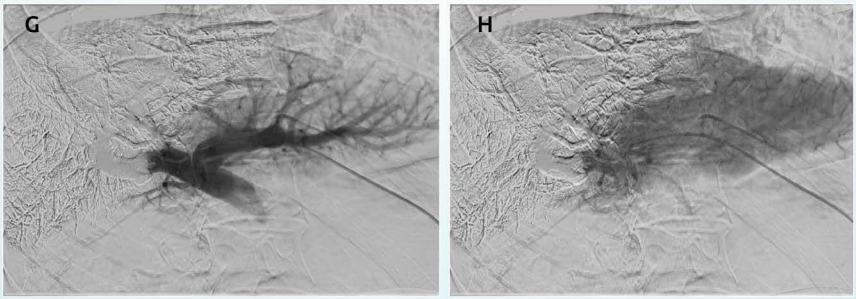


Figure 35 GH

while removing the microcatheter at the same time in order to generate reflux. As you may have noticed, this is a different technique that relies on reflux to reach the other branches and complete the embolization. If needed, you can flush the catheter on the table and go back to embolize a different branch. The kind of embolization you will achieve using this method is very distal. Pay attention to the proximal port, especially when using a 1:8 ratio. An alternative is to prepare two different dilution rates, 1:8 for the distal port and 1:1 for the proximal port, although it is not necessary to embolize the proximal port. Concerning quantity, 9 ml is most likely enough in this case. The procedure is fast and easy and the result completely satisfactory. Flushing directly in the 5 F catheter is a possibility, provided that we make sure there is no glue on the tip lest we run the risk of leaving glue in the left port in the process of removing the catheter. A coaxial technique is always safer to manage.

The evidence from the randomized study has now proved that glue is the best embolic agent for portal vein embolization.

Gastrointestinal bleeding

Over the past five years, the literature concerning gastrointestinal bleeding shows that glue is the most often employed embolic agent in this kind of indication, especially in Asian countries [8-11]. We have recently published a meta-analysis on the subject [2]. How distal does Lower GastroIntestinal Bleedings (LGIB) need to be?

– Superselective
- Jejunum, ileum, colon
- Distal embolization of vasa recta (straight artery)
- Beyond the marginal artery
- As close as possible to the site of hemorrhage
- Bowel wall ischemia is unlikely
  - 3 or fewer vasa recta: not risky / - 4 or more vasa recta: risky

In the discussion as to how to avoid ischemic complications (Fig.36), especially in relation to the lower gastrointestinal part, the factor that needs to be taken into account is the number of vasa recta we embolize. The risk is next to none when we embolize up to three vasa recta. In 2017, JVIR published a notable meta-analysis on the subject [3]. The pooled clinical success and major complication rates in the 259 patients with UGIB in whom technical success was achieved were 82.1% and 5.4%, respectively, and those in the 175 patients with LGIB in whom technical success was achieved were 86.1% and 6.1%, respectively (Fig.37).

- 440 patients
- 13 ischemic complications: 2.9%
- Only 3 needed bowel resection (Fig.38)

How to avoid ischemic complication

We can certainly say that there is no high risk of ischemic complications in

How to avoid ischemic complications?

- How distal does LGIB need to be?
  - Superselective
    - Jejunum, ileum, colon
    - Distal embolization of vasa recta (straight artery)
    - Beyond the marginal artery
    - As close as possible to the site of hemorrhage
    - Bowel wall ischemia is unlikely
      - 3 or fewer vasa recta: not risky
      - 4 or more vasa recta: risky

Experimental Study on Acute Ischemic Small Bowel Changes Induced by Superselective Embolization of Superior Mesenteric Artery Branches with *N*-Butyl Cyanoacrylate

Hwan Jun Jae, MD, Jin Wook Chung, MD, Hyo-Cheol Kim, MD, Yeong Ho So, MD, Hyung Guhn Lim, MD, Whal Lee, MD, Byoung-Kwon Kim, MD, and Jae Hyung Park, MD

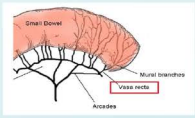


Figure 36 - Avoiding ischemic complications

CLINICAL STUDY

Transcatheter Arterial Embolization of Gastrointestinal Bleeding with *N*-Butyl Cyanoacrylate: A Systematic Review and Meta-Analysis of Safety and Efficacy

Pyeong Hwa Kim, MD, Jiaywei Tsauo, MD, Ji Hoon Shin, MD, and Sung-Cheol Yun, PhD

440 patients

13 ischemic complications: 2.9%

Only 3 needed bowel resection

Table E6. List of Patients with Major Complications

Pt. No./Age (y)/Sex	Site of Bleeding	Etiology of Bleeding	Embolic Agent	Embolized Artery	Complication	Management	Outcome
				UGIB			
1/55/F	Stomach	Ulceration	Histoacryl	LGA	Ulceration	Conservative treatment	Recovered
2/90/F	Stomach	Malignancy	Histoacryl	LGA	Ulceration	Conservative treatment	Recovered
3/73/M	Stomach	Ulceration	Histoacryl	LGA	Ulceration	Conservative treatment	Recovered
4/77/M	Duodenum	Ulceration	Histoacryl, coils	GDA	Liver infarction	Conservative treatment	Recovered
5/67/M	Duodenum	Iatrogenic injury	Histoacryl	APDA	Bowel infarction	Conservative treatment	Died of perforation 6 wk later
				LGIB			
1/79/F	GJ anastomosis	Iatrogenic injury	Histoacryl	JA	Ulceration	Conservative treatment	Recovered
2/65/M	GJ anastomosis	Iatrogenic injury	Histoacryl	JA	Bowel infarction	Bowel resection	Recovered
3/56/F	Jejunum	Malignancy	Histoacryl	JA	Bowel infarction	Conservative treatment	Recovered
4/59/M	Appendix	–	Histoacryl	AA	Bowel infarction	Bowel resection	Recovered
5/50/M	Appendix	Trauma	Histoacryl	AA	Bowel infarction	Bowel resection	Recovered
6/52/M	Appendix	Diverticulosis	Histoacryl	ICA	Bowel infarction	Conservative treatment	Recovered
7/79/M	Colon	Diverticulosis	Histoacryl	RCA	Ulceration	Conservative treatment	Recovered
8/66/M	Colon	Diverticulosis	Histoacryl	ICA	Ulceration	Conservative treatment	Recovered

Figure 37

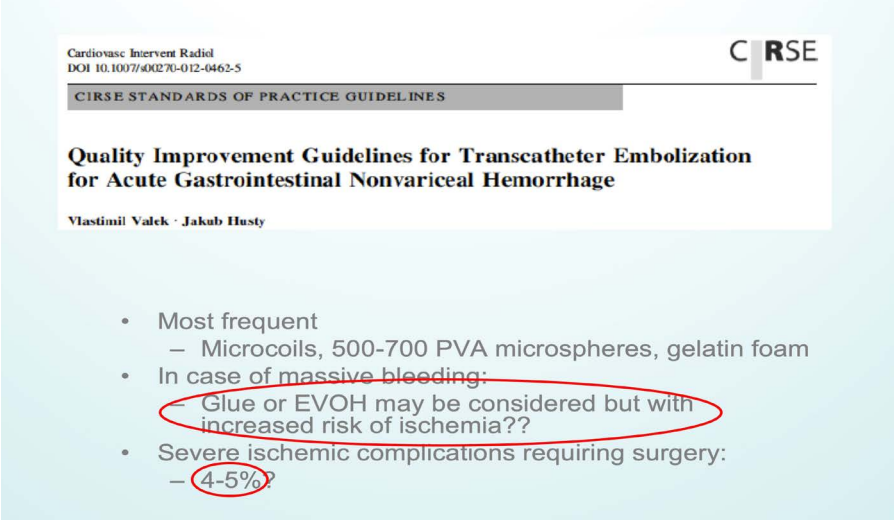


Figure 38

the use of glue for this indication, disregarding the location. If we look at the Cirse guidelines [12], microcoils and particles are indicated as the most frequently employed embolic agents. In case of massive bleeding: "*Glue or EVOH (copolymers) may be considered but with increased risk of ischemia*". We believe this statement to be false, as the game-changing factor is in fact the number of vasa recta we embolize, not the embolic agent we choose. Additionally, severe ischemic complications requiring surgery are indicated as 4-5%, while the meta-analysis indicates in fact 2.9% (Fig.38).

We can conclude that, when compared to other embolic agents, in GI bleedings glue does not pose a higher risk of ischemic complications.

When we perform an empirical embolization, with or without extravasation, we can locate the bleeding ulcera through an endoscopy and then proceed with embolizing the gastroduodenal artery (GDA) (Figs.39-41). We usually put coils in the right gastroepiploic artery (GEA) to protect it and prevent distal embolization by liquids. It is now safe to inject the glue in the rest of the trunk and

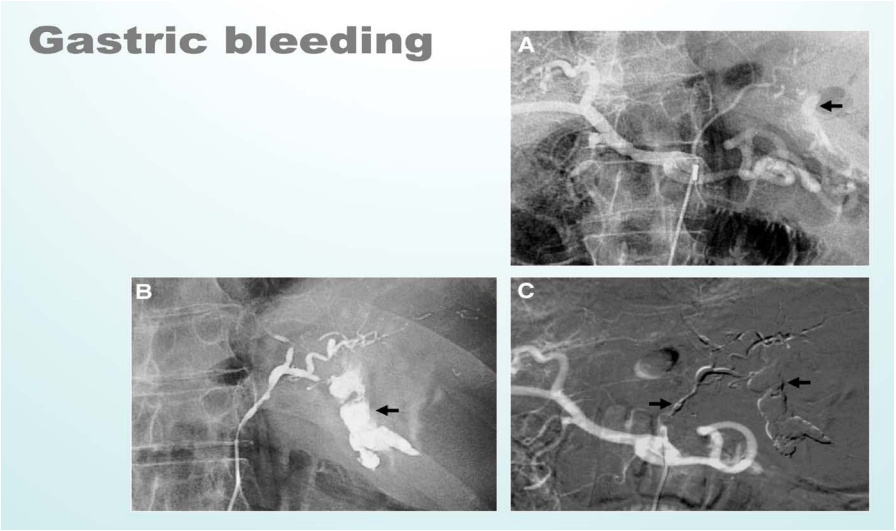


Figure 39

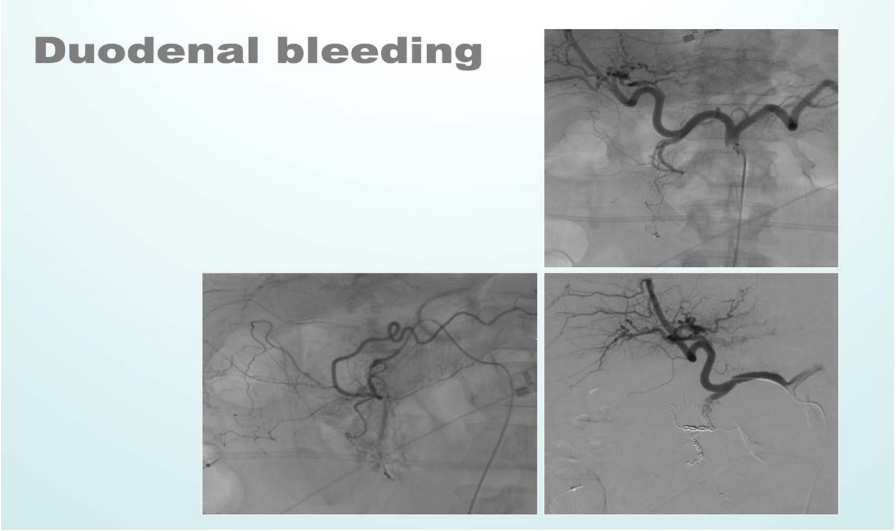


Figure 40

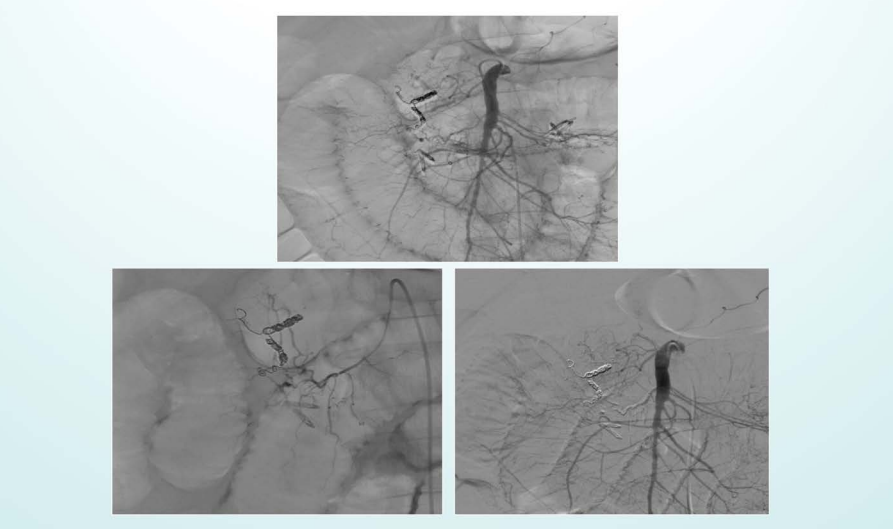


Figure 41

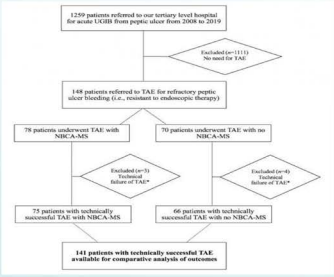
the branches. Because we need to avoid migration in case of reflux, we use a 1:1 dilution ratio and start to form the cast by slowly injecting the mixture while removing the microcatheter. We published many papers on GDA bleeding, showing that it is always preferable to use a combination of agents, however, when only one embolic agent is employed, glue gives the best results. Several studies have shown the superiority of NBCA versus other embolic agents for both upper and lower GI bleedings in terms of clinical outcomes, with less of rebleeding, especially in patients with coagulation disorders (Figs. 42-45) [13].

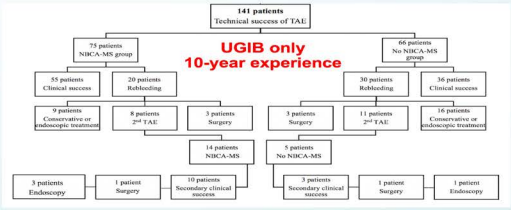
Extravasation control

It is important to always check the superior mesenteric artery for extravasation. With so many collaterals, there is no danger of ischemic complications, however, an incomplete embolization may pose serious risk of rebleeding, as most of these patients have comorbidities or take anticoagulants. For this reason, we perform a very aggressive embolization in these cases, to ensure

The evidence for UGIB

Largest comparative study: NBCA *vs* others





> Eur Radiol. 2021 May;31(5):3018-3026. doi: 10.1007/s00330-020-07427-y. Epub 2020 Oct 31.

Ten-year experience with arterial embolization for peptic ulcer bleeding: N-butyl cyanoacrylate glue versus other embolic agents

Romaric Loffroy [1 2], Anne-Solène Desmyttere [3], Thomas Moulliet [4], Julie Pellegrinelli [2], Olivier Facy [4], Antoine Drouillard [4], Nicolas Falvo [3], Pierre-Emmanuel Charles [3], Marc Bardou [4], Marcie Mbula [3], Serge Aho-Glélé [1], Olivier Chevallier [3]

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Figure 42

Higher clinical success/ shorter procedure

	Overall (n = 148)	NBCA-MS (n = 78)	No NBCA-MS (n = 70)	*P* value
Technical success	141 (95.3)	75 (96.2)	66 (94.3)	.708
Primary 30-day clinical success*	94/148 (63.5)	55/75 (73.3)	36/66 (54.5)	**.023**
Rebleeding <30 days	54/148 (36.5)	20/75 (26.7)	30/66 (45.5)	**.023**
Time to rebleeding (days)	7.8±15.9 (0-90)	10.5±23.1 (0-90)	7.0±9.8 (0-40)	.752
Management of early rebleeding				
Conservative	24/54 (44.4)	9/20 (45.0)	16/30 (53.3)	.773
Repeat embolization	19/54 (35.2)	8/20 (40.0)	11/30 (36.7)	.999
Surgery	11/54 (20.4)	4/20 (20.0)	4/30 (13.3)	.697
After 1 TAE	9/54 (16.7)	3/20 (15.0)	3/30 (10)	.672
After 2 TAEs	2/54 (3.7)	1/20 (5.0)	1/30 (3.3)	.468
Secondary clinical success	42/54 (77.8)	10/14 (71.4)	3/5 (60.0)	.999
Day-30 mortality	32/148 (21.6)	19/75 (25.3)	11/70 (16.7)	.224
Related to UGIB	15/148 (10.1)	6/75 (8.0)	7/70 (10.6)	.132
Unrelated to UGIB	17/148 (11.5)	13/75 (17.3)	4/70 (6.1)	.132
Overall hospital stay length (days)	23.7±30.8 (2-180)	19.7±25.8 (2-180)	20.4±28.0 (2-159)	.508
Fluoroscopy time (min)	26.8±18.8 (5.5-120)	20.8±11.5 (5.5-61)	35.5±23.4 (6.2-120)	**.002**
Periprocedural complications**	19/148 (12.8)	8/75 (10.7)	6/66 (9.1)	.786
Minor	8/148 (5.4)	6/75 (8.0)	2/66 (3.0)	.283
Major	11/148 (7.4)	2/75 (2.7)	4/66 (6.1)	.419

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Figure 43

NBCA as an independent Prognostic factor

	Rebleeding			Death		
	Univariate	Multivariate analysis		Univariate	Multivariate analysis	
Parameters	***P-value***	***OR (95%CI)***	***P-value***	***P-value***	***OR (95%CI)***	***P-value***
Age	.429	-	-	**.114**	10.01 (0.98-10.05)	.450
Sex	**.189**	0.64 (0.28-10.46)	.201	.659	-	-
Initial hemoglobin	.984	-	-	**.001**	10.38 (10.10-10.74)	**.006**
Total PRBC transfusion	.798	-	-	.767	-	-
Medications						
Antiplatelet agent	**.107**	20.20 (0.90-50.41)	.085	.595	-	-
Anticoagulant therapy*	.826	-	-	.201	-	-
Both	.458	-	-	.999	-	-
NSAIDs	.999	-	-	.146	-	-
≥ 2 comorbidities	**.033**	20.14 (10.01-40.52)	**.047**	**.041**	20.14 (0.84-50.50)	.112
Coagulopathy**	.848	-	-	.657	-	-
No. of endoscopies before TAE	.412	-	-	**.194**	10.31 (0.82-20.11)	.261
Forrest classification***						
Forrest I	.999	-	-	.518	-	-
Forrest II	.999	-	-	.999	-	-
Forrest III	.999	-	-	.453	-	-
Time from refractory bleeding onset to angiography	.924	-	-	.330	-	-
Contrast extravasation	.592	-	-	.530	-	-
Embolized vessel						
GDA	.999	-	-	.594	-	-
LGA	.418	-	-	.523	-	-
RGA	.347	-	-	.584	-	-
LGEA	.615	-	-	**.002**	-	-
SMA	**.053**	-	-	**.065**	-	-
NBCA-MS	**.023**	0.47 (0.22-0.99)	**.047**	.224	10.37 (0.55-30.37)	.498
Alone	.137	0.30 (0.09-10.02)	.053	.999	0.82 (0.22-30.10)	.765
Combined with coils	**.151**	0.78 (0.36-10.67)	.520	.206	10.51 (0.61-30.73)	.374
No.NBCA-MS	**.023**	20.15 (10.01-40.56)	**.047**	.224	0.73 (0.30-10.81)	.498
Coils only	**.030**	20.40 (10.13-50.14)	**.024**	.532	0.88 (0.34-20.25)	.786
Other embolic agents	.754	0.75 (0.10-50.27)	.685	.457	0.43 (0.04-40.36)	.471

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Figure 44

The evidence for LGIB

Superselective transcatheter arterial embolization for acute small bowel bleeding: clinical outcomes and prognostic factors for ischemic complications

Yong Seok Kim[1,2], Joon Ho Kwon[1], Kichang Han[1], Man-Deuk Kim[1], Junhyung Lee[1], Gyoung Min Kim[1] and Jong Yun Won[1]

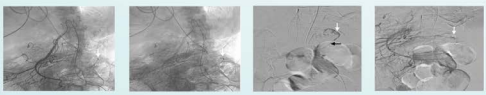
2020

Superselective embolisation and the **use of NBCA** were **significant prognostic factors** associated with **reduced recurrent bleeding** and **fewer major complications,** independently

74 patients

Table 4. Univariate and Multivariate Analysis of Various Prognostic Factors for Clinical Outcomes.

	Univariate		Multivariate	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Complication				
Recent GI surgery	0.164 (0.020–1.348)	0.093	0.097 (0.009–1.098)	0.059
Superselective embolization	0.099 (0.027–0.368)	0.001	0.069 (0.012–0.406)	0.003
Embolization materials (NBCA)	0.257 (0.077–0.859)	0.027	1.303 (0.221–7.674)	0.770
In-hospital mortality				
Enteritis	0.153 (0.019–1.253)	0.080	0.791 (0.636–0.981)	0.034
Hemodynamic instability	11.636 (2.428–55.764)	0.002	1.391 (1.153–1.679)	0.001
Inotropics use	3.250 (1.077–9.803)	0.036	1.142 (0.933–1.397)	0.192
Hemoglobin level (< 7)	1.450 (1.220–1.723)	0.015	1.069 (0.829–1.380)	0.602
Bleeding focus (jejunum)	2.969 (0.990–8.900)	0.052	1.154 (0.952–1.399)	0.141



2019

Transcatheter arterial embolisation for acute lower gastrointestinal haemorrhage: a single-centre study

134 patients

Figure 45

we will not need to intervene a second time at a later stage.
Whether we were dealing with recanalization or with a known event previously shown by the initial angiography, the extravasation was evident and made it difficult to approach more distally. We used a 1:3/1:4 ratio and achieve great results. Regarding a left colon extravasation from the inferior mesenteric artery, the risk of recanalization is high, as it is impossible to reach behind the extravasation to perform a sandwich embolization with the aid of coils. This is what we call a blocked flow embolization, where glue is the perfect choice as it allows for total control.
The mixture will advance when we push and it will stop when we stop injecting. By using hyperpressure, we can easily push the glue beyond the extravasation point and reach the two vasa recta we need to embolize. The feeling is that of a microcatheter with an occlusive balloon: we want to avoid reflux so we push slowly and distally. We do not actually need a balloon, the microcatheter is enough to block the flow, as you can see in this case of diverticular bleeding (Fig.46). This is another example of extravasation from trauma, in a spastic patient (Fig. 47) [14]. The artery is small and the extravasation quite large, however, we can sacrifice the branch without concern. Two drops of glue are enough here and the the dilution ratio is not important. Due to the spasticity and the bleeding, it is easy to underestimate the size of the coils and cause the artery to reopen at a later time. Figures 48 A-F show a complicated case of hepatocellular carcinoma (HCC) bleeding with occlusion of the celiac trunk involving the superior mesenteric artery and the pancreatic duodenal arcades. Chemoembolization would appear the perfect step to follow such a procedure, however, it is not necessary. The patient can be fully treated through a simple embolization performed by using a 1:6 dilution ratio, and closing the access for any future chemoembolization will not be an issue. At follow-up, we observed perfect necrosis and the patient was admitted for surgery. After five years, the patient is alive and doing well. In this particular indication, the chemotherapeutic agent in chemoembolization is only accessory to the embolization itself, and you can sacrifice the branch with-

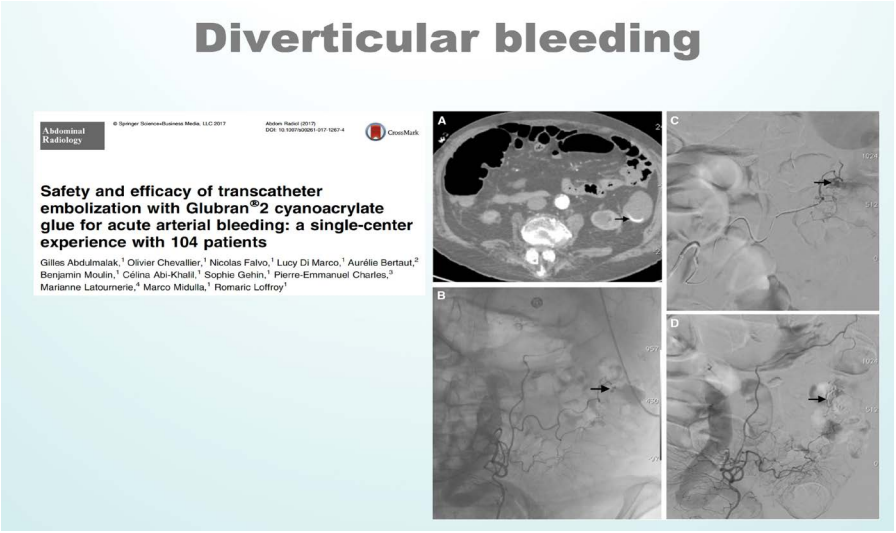


Figure 46 - Diverticular bleeding

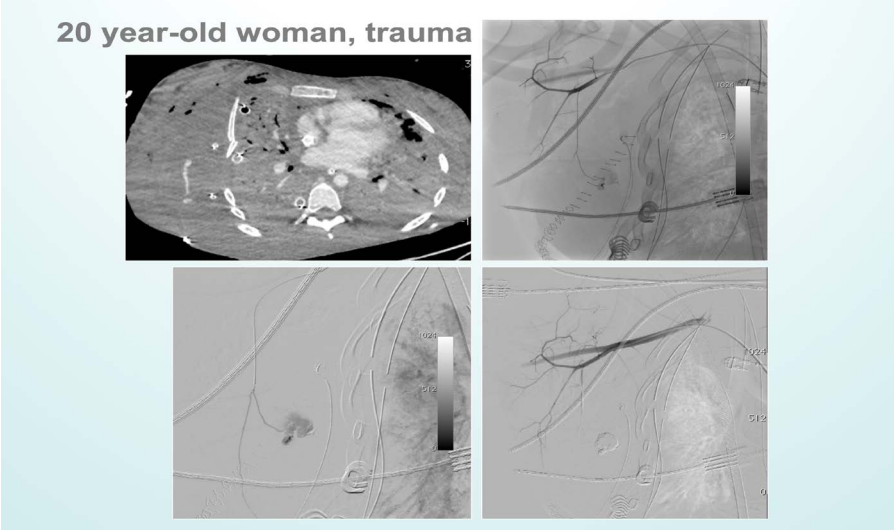


Figure 47 - 20 year-old woman, trauma

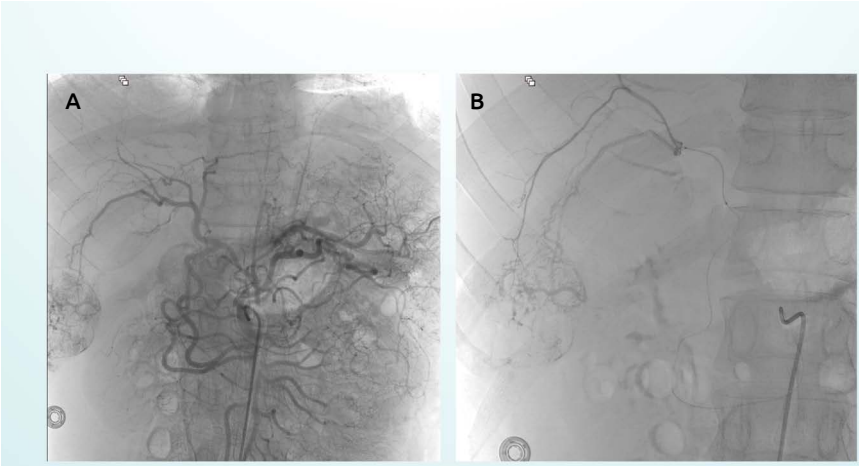


Figure 48 AB - HCC rupture

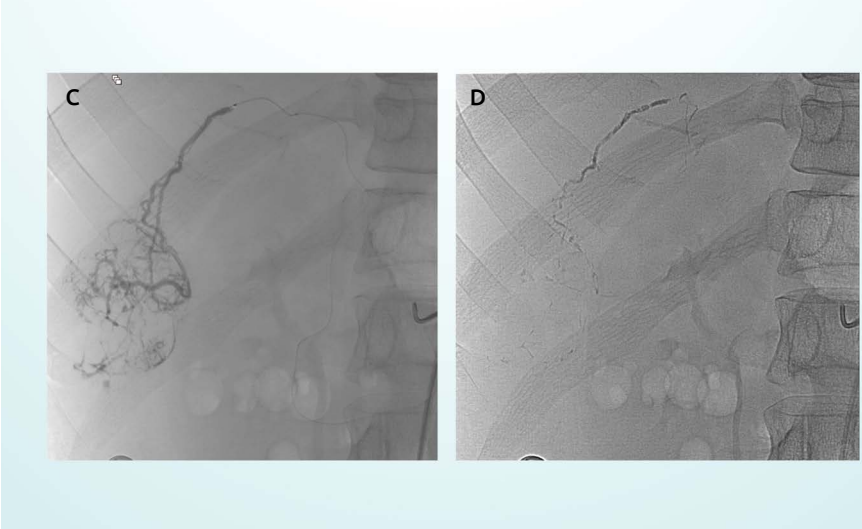


Figure 48 CD

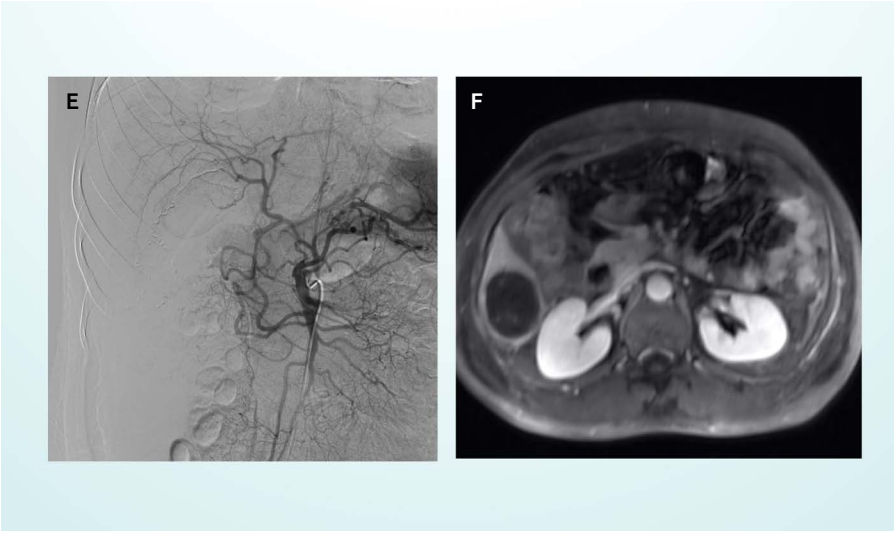


Figure 48 EF

out concern and achieve the best possible outcome. In case of pseudoaneurysm in the splenic artery, we know we can expect an infarction as a likely consequence, disregarding the embolic agent of choice. Nevertheless, the size of the infarction may be affected by the number of microcoils employed to complete the embolization. Once again, liquids appear to be the safest solution. Recently, patients on anticoagulants who arrive in our practice with spontaneous bleeding have been more and more frequent; this is a complicated indication, as we cannot treat the patient directly, but we have to rely on images [15]. Sometimes, we can only detect a small hematoma and the patient seems to be recovering well, however, the size of the hematoma represents a prognostic factor in itself. In case of internal extravasation, we find that the best choice is to perform a preventive embolization, as the hematoma is likely to grow, causing both venous and arterial bleeding that are not easy to control when it is too late. By using a 1:3/1:4 dilution ratio we can perform a quick embolization and sacrifice the entire branch to prevent complications that can take

as little as one hour to arise. Undoubtedly, age is an important factor in the rate of the growth and we are aware that this is more likely to happen in patients who are over 70 years old. Nonetheless, if the CT scan detects an active bleeding with extravasation, we do not foresee it is likely to stop spontaneously. Even when we decide to administer antagonists, for example, we know they take several hours to work, so we proceed with embolizing at the same time, to prevent the hematoma from growing. In 50 patients who underwent Glubran® 2 embolization, we observed a 40% mortality rate at one month: clinicians are possibly unaware of such outcome and often put patients on anticoagulant even when they are not strictly necessary. While these medications can save lives, they can also cause death. In patients who are being treated with antiplatelet or anticoagulant, we see spontaneous bleeding in absence of trauma, and the hematoma grows bigger every time. At least in case of extravasation, preventive embolization is, in our opinion, the safest choice, even when the patient conditions seem to be improving (Fig. 49) [14].

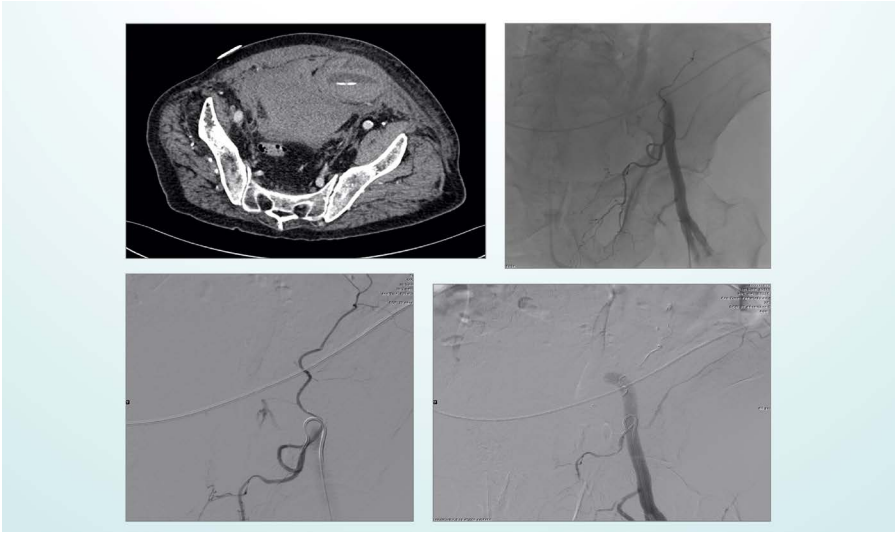


Figure 49

Prostatic embolization

A very interesting indication we recently published about is **prostatic artery glue embolization for adenoma** (Figs. 50-56) [16-18].
We tried to create a blocked flow environment and that is why we preferred a 2.7 F microcatheter. We positioned the tip as far as possible and then injected a 1:8 ratio mixture. Observe the cast travelling distally and the even distribution. This is a 50 patients safety study and, from a clinical perspective, the results are comparable to those indicated by the literature on the use of microparticles.
I personally recently reviewed a paper about a retrospective study on particle embolization versus glue embolization. While the complication rate derived by the use of glue was not considerably lower, what was significant was the difference in radiation exposure. This is due to the simple fact that glue embolization is a much faster procedure. Naturally, catheterism is the most challenging part of this kind of procedure, disregarding the agent of choice, but embolization with microparticles takes about 15 minutes for each side, whereas glue only takes a few seconds to work, and that significantly reduces radiation exposure. Moreover, when we have collaterals, we do not want to embolize, we can occlude them with a cast of glue and push again in the gland, which is not possible with particles. In some cases, if we cannot occlude the proximal port of the collaterals with coils, we cannot perform the embolization. **Glue will work in any situation, especially in a blocked flow scenario**, because when you push some glue very slowly at the proximal port of the collateral and then wait a short time, you will be able to push again in the main branch into the gland with no risk of penile non-target embolization.

Journal of Clinical Medicine
MDPI
Article

Prostate Artery Embolization Using N-Butyl Cyanoacrylate Glue for Urinary Tract Symptoms Due to Benign Prostatic Hyperplasia: A Valid Alternative to Microparticles?

Romaric Loffroy [1,*], Kévin Guillen [1], Etienne Salet [2], Clément Marcelin [2], Pierre-Olivier Comby [3], Marco Midulla [1], Nicolas Grenier [2], Olivier Chevallier [1] and François Petitpierre [2]

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Table 3. PAE efficacy outcomes after 3 months.

Variables	Baseline	3 Months	Change (%)	*p* Value
IPSS				
Mean ± SD	20.5 ± 6.7	9.9 ± 6.8	−10.6 (51.7)	0.0001
Median (IQR)	20.5 (16.7–25)	8.0 (5.3–13.0)	−12.5 (61.0)	
QoL score				
Mean ± SD	4.9 ± 1.0	2.2 ± 1.5	−2.7 (55.1)	0.0001
Median (IQR)	5.0 (4.0–6.0)	2.0 (1.0–3.0)	−3 (60.0)	
IIEF5				
Mean ± SD	16.2 ± 7.5	15.8 ± 7.9	−0.4 (2.5)	0.078
Median (IQR)	17.5 (11.0–23.0)	18.0 (10.0–23.0)	+0.5 (2.8)	
PSA (ng/mL)				
Mean ± SD	6.4 ± 3.7	4.6 ± 3.0	−1.8 (28.1)	0.0001
Median (IQR)	5.6 (4.0–7.6)	4.1 (2.3–5.9)	−1.5 (26.8)	
Prostate volume (mL)				
Mean ± SD	98.3 ± 40.2	77.3 ± 30.5	−21 (21.4)	0.0001
Median (IQR)	91.2 (67.6–122.3)	70.7 (57.7–94.6)	−20.5 (22.5)	

IQR, interquartile range; IPSS, International Prostatic Symptoms Score; QoL, quality of life; IIEF5, International Index of Erectile Function; PSA, prostate-specific antigen. *p* values < 0.05 were considered statistically significant.

Figure 50

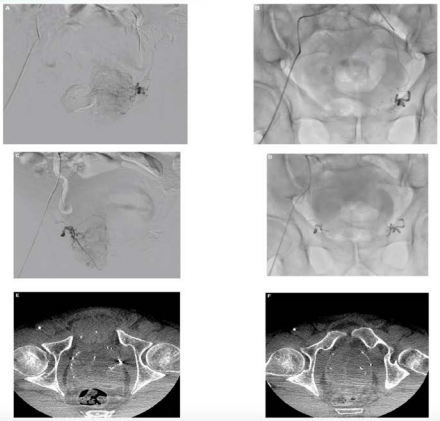


Table 2. Technical features of PAE and short-term safety outcomes.

Variables	Data
Arterial approach, *n* (%)	
Left radial	11 (22.0)
Right femoral	39 (78.0)
Type of embolization, *n* (%)	
Unilateral	3 (6.0)
Bilateral	47 (94.0)
Number of embolized arteries, *n* (%)	
1	3 (6.0)
2	37 (74.0)
3	10 (20.0)
Total injected embolic mixture [a] volume, mL	
Mean ± SD	0.9 ± 0.3
Median (IQR)	0.8 (0.6–1.1)
Total mixture [a] injection time, s	
Mean ± SD	21.9 ± 7.8
Median	20.5 (15.3–27.5)
Total PAE duration, min	
Mean ± SD	95.0 ± 29.0
Median	93 (80–120)
Fluoroscopy duration, min	
Mean ± SD	27.5 ± 11.3
Median	23.7 (19.6–33.5)
Radiation dose (mGy·cm)	
Mean ± SD	18 458 ± 16 397
Median (IQR)	14 907 (8 947–24 000)
Technical success [b], *n* (%)	50 (100.0)
Clinical success [c], *n* (%)	43 (86.0)
Complications according to SIR [d], *n* (%)	
Minor	11 (22.0)
A	9 (18.0)
B	2 (4.0)
Major	0 (0.0)
Clavien–Dindo score, *n* (%)	
I	9 (18.0)
II	2 (4.0)
Follow-up (months)	
Mean ± SD	4.7 ± 5.0
Median (IQR)	3.0 (3.0–5.0)

IQR, interquartile range; SIR, Society of Interventional Radiology; [a] Mixture of N-butyl cyanoacrylate and Lipiodol Ultra Fluid. [b,c,d] At median follow-up (3 months).

Figure 51

Figure 52

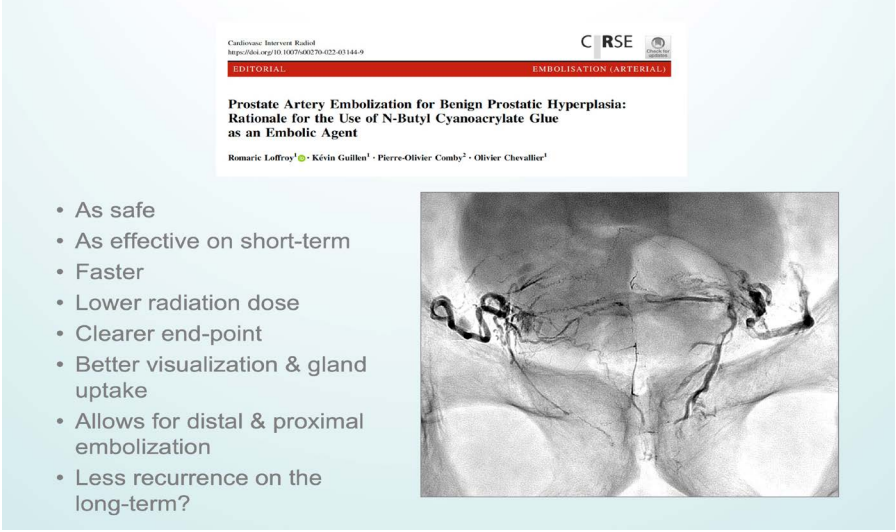


Figure 53

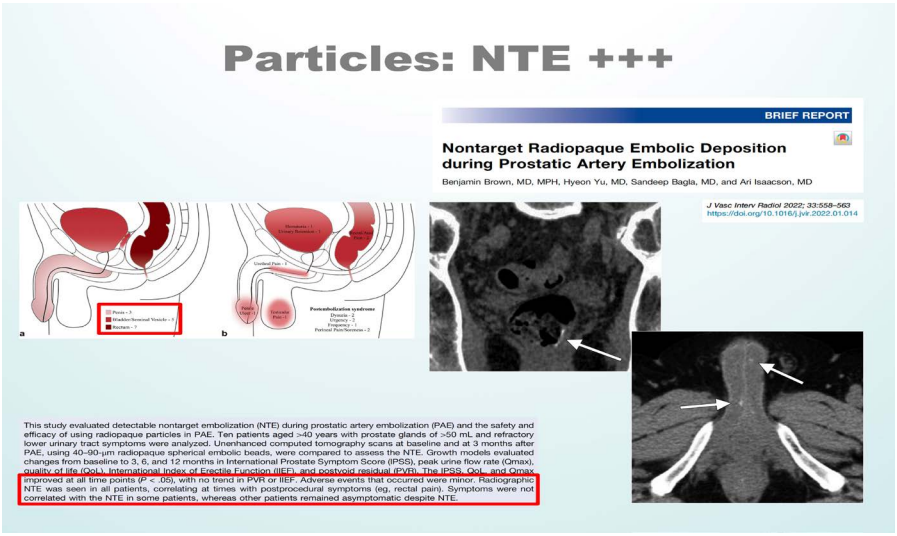


Figure 54

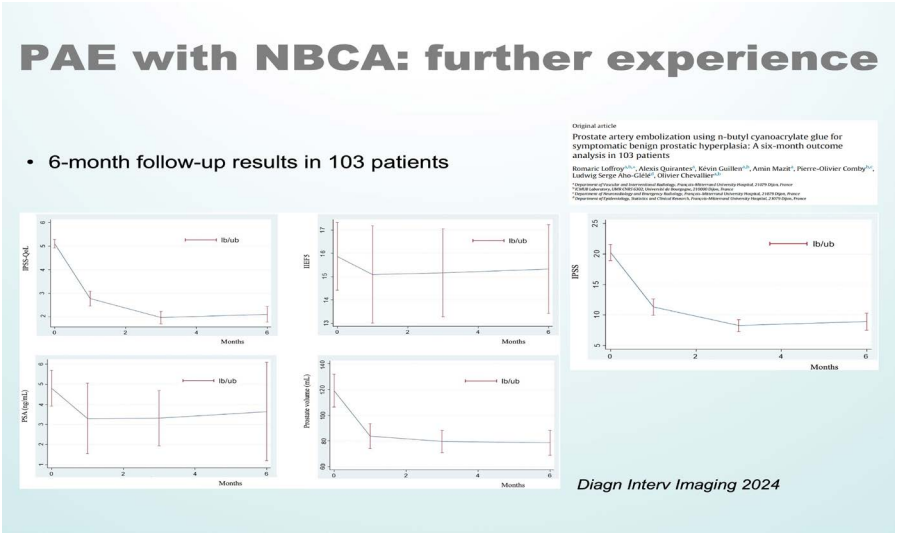


Figure 55

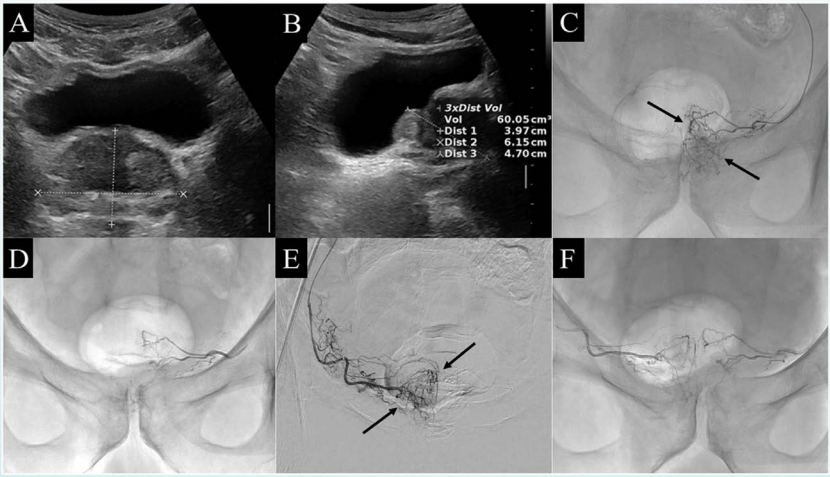

A
B
C
D
E
F
3xDist Vol
Vol 60.05 cm³
Dist 1 3.97 cm
Dist 2 6.15 cm
Dist 3 4.70 cm
Loffroy et al. Diagn Interv Imaging 2024

Figure 56

Varicocele

In another study we compared different groups using several embolic agents, such as Glubran® 2, polidocanol, and coils (Fig. 57)[19]. Our study concluded as follows: "***The use of Glubran® 2 acrylic glue for varicocele embolization is safe and leads to less radiation and lower recurrence rates than is the case for other embolic materials without any more significant pain***" (Figs.58,59)[20]. This is a typical distal embolization performed with a 5 F catheter. As shown in the picture, the standard goal is usually to embolize from point A to point B, which we believe is a mistake, since revascularization and recurrence always involve the saphenous branch below the iliopectineal line. Disregarding the difference in branches, we always have anastomosis behind this point, and this is why we prefer to embolize from point C to point A. We place the microcatheter at point C and start injecting a 1:1 ratio mixture while retracting the microcatheter until the embolization is complete and we can remove it. When it is not possible to place the microcatheter far enough, we can exploit the features of liquids by placing the tip at point A and ask the patient for Valsalva. This will help the glue to travel distally, all the way down to point C. In case of reflux at the tip, make sure you do not immediately remove the microcatheter, but wait for polymerization to start and withdraw the microcatheter after about 5 minutes[18].

biomedicines

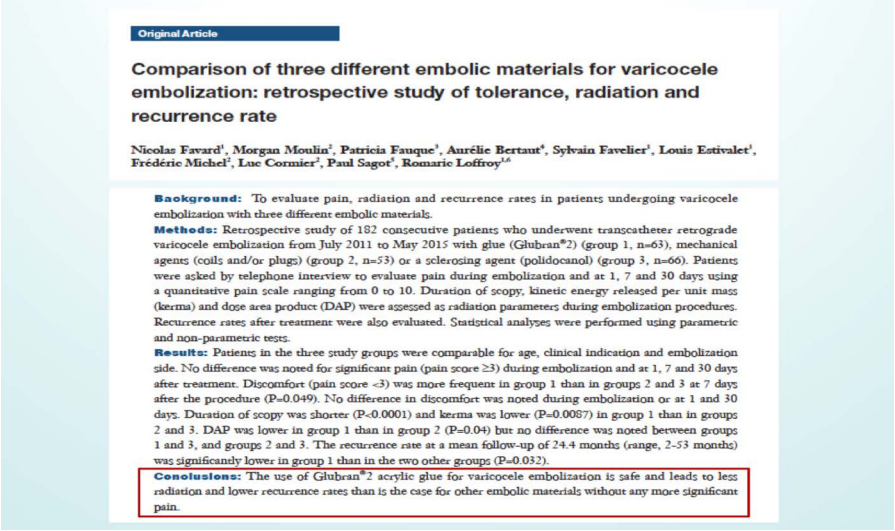
MDPI

Article

Relevant Biological Effects of Varicocele Embolization with N-Butyl Cyanoacrylate Glue on Semen Parameters in Infertile Men

Olivier Chevallier [1,2], Patricia Fauque [3], Carole Poncelet [4], Kévin Guillen [1,2], Pierre-Olivier Comby [2,5], Karine Astrue [6], Julie Barberet [7], Nicolas Falvo [1], Emmanuel Simon [7] and Romaric Loffroy [1,2,*]

Figure 57



Original Article

Comparison of three different embolic materials for varicocele embolization: retrospective study of tolerance, radiation and recurrence rate

Nicolas Favard[1], Morgan Moulin[2], Patricia Fauque[3], Aurélie Bertaut[4], Sylvain Favelier[1], Louis Estivalet[1], Frédéric Michel[2], Luc Cormier[2], Paul Sagot[5], Romaric Loffroy[1,6]

Background: To evaluate pain, radiation and recurrence rates in patients undergoing varicocele embolization with three different embolic materials.

Methods: Retrospective study of 182 consecutive patients who underwent transcatheter retrograde varicocele embolization from July 2011 to May 2015 with glue (Glubran®2) (group 1, n=63), mechanical agents (coils and/or plugs) (group 2, n=53) or a sclerosing agent (polidocanol) (group 3, n=66). Patients were asked by telephone interview to evaluate pain during embolization and at 1, 7 and 30 days using a quantitative pain scale ranging from 0 to 10. Duration of scopy, kinetic energy released per unit mass (kerma) and dose area product (DAP) were assessed as radiation parameters during embolization procedures. Recurrence rates after treatment were also evaluated. Statistical analyses were performed using parametric and non-parametric tests.

Results: Patients in the three study groups were comparable for age, clinical indication and embolization side. No difference was noted for significant pain (pain score ≥3) during embolization and at 1, 7 and 30 days after treatment. Discomfort (pain score <3) was more frequent in group 1 than in groups 2 and 3 at 7 days after the procedure (P=0.049). No difference in discomfort was noted during embolization or at 1 and 30 days. Duration of scopy was shorter (P<0.0001) and kerma was lower (P=0.0087) in group 1 than in groups 2 and 3. DAP was lower in group 1 than in group 2 (P=0.04) but no difference was noted between groups 1 and 3, and groups 2 and 3. The recurrence rate at a mean follow-up of 24.4 months (range, 2–53 months) was significantly lower in group 1 than in the two other groups (P=0.032).

Conclusions: The use of Glubran®2 acrylic glue for varicocele embolization is safe and leads to less radiation and lower recurrence rates than is the case for other embolic materials without any more significant pain.

Figure 58

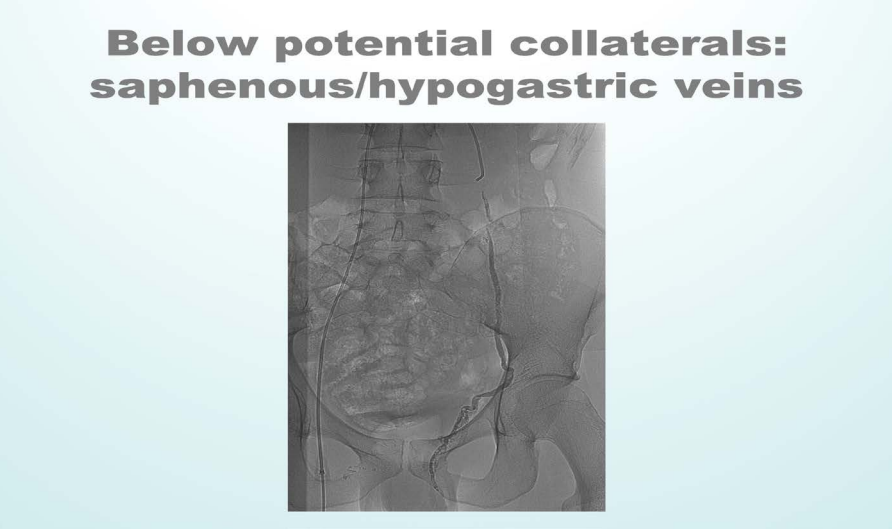

Below potential collaterals:
saphenous/hypogastric veins

Figure 59

Pelvic congestion syndrome (PCS): connection with internal iliac artery (IIA)

The goal in this case is to embolize the reservoir in order to achieve a distal embolization (Fig. 60). The steps here are to first put one or two coils at the proximal port, go through the coils with the microcatheter, inject the glue from the distal port, and ask the patient for Valsalva while removing the catheter until we reach the coils.
In women varices are normally very large and the cast of glue in case of reflux can be less easily controlled so we use the coils not to occlude but to protect. A possible reflux would be trapped by the coils.

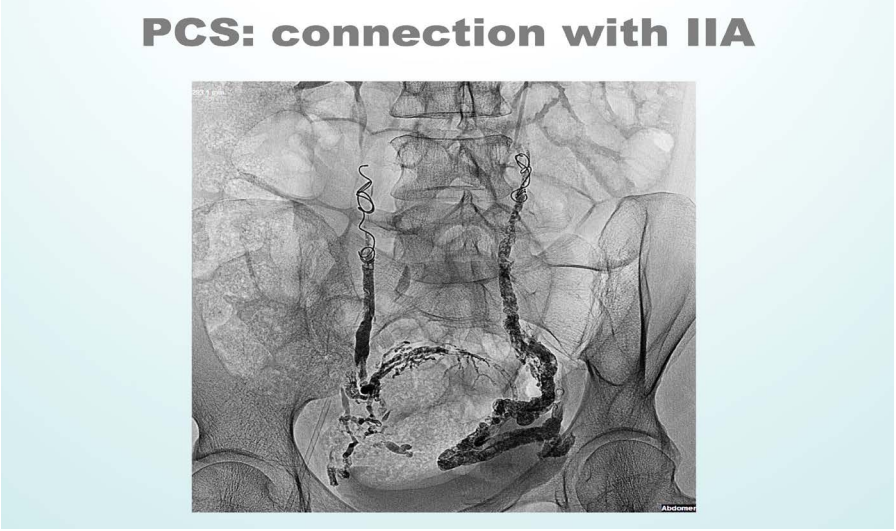


Figure 60

False aneurysm at the common femoral artery

Here we have a false aneurysm at the common femoral artery (Figs.61,62). In this case we need additional access, as it is mandatory to place a balloon in front of the neck in order to prevent reflux that would be seriously difficult to handle.
After placing the balloon, we inject the glue directly in the sack using the metallic needle and, under fluoroscopy, we fill the sack using a 1:1 mixture. We wait about 5 minutes before deflating the balloon. Always perform a thorough check to ensure nothing is left in the artery. A 0.035" balloon poses no risk of sticking or bursting (Fig.63).

Figure 61

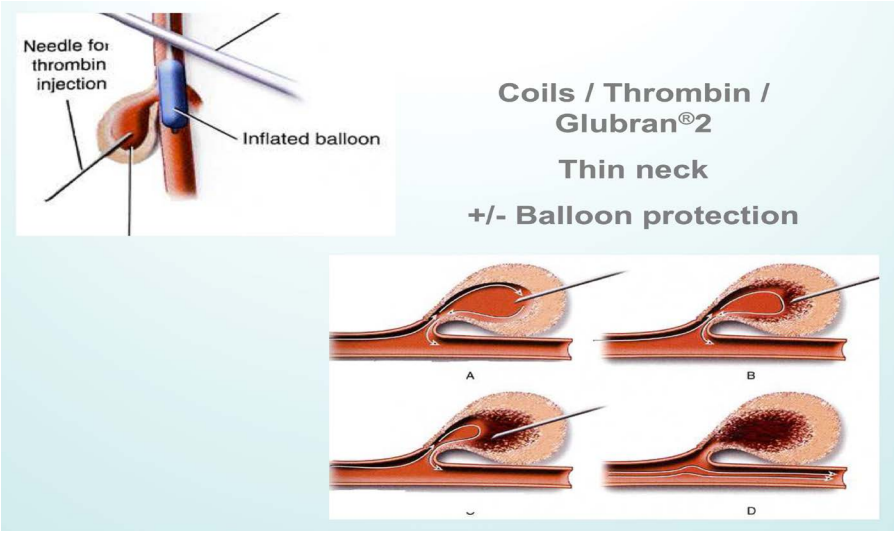


Figure 62

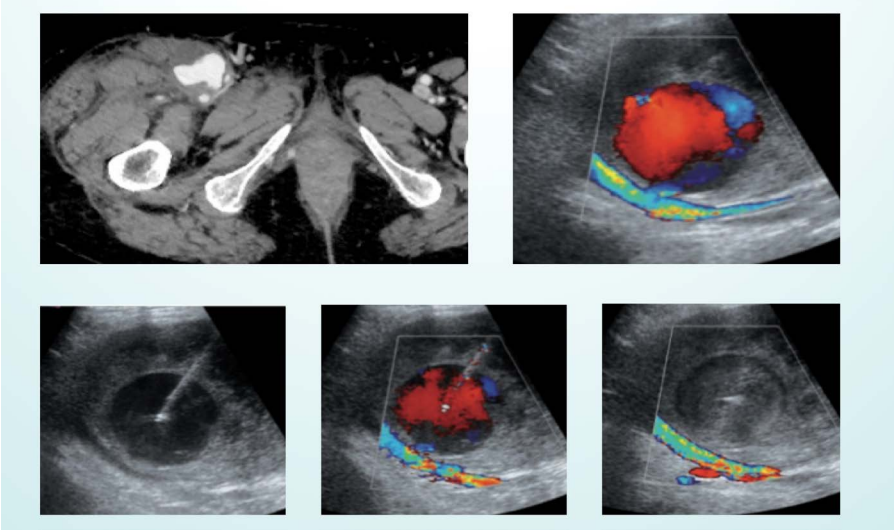


Figure 63

Conclusions

In conclusion, **liquids have proved extremely useful and versatile, despite the learning curve**. We have assessed that the risk rate for non-target embolization or reflux is comparable to using microparticles. As this is a one-shot embolization, we need to be confident.
The goal of this workshop is chiefly to dispel any doubt related to sticking the catheter: do not fear a little extra adherence, as this is not a real issue.
Among the many agents at our disposal, **the combination Glubran®2 / Ethiodized Oil has proved to be the fastest and easiest option in many indications**.

Take home messages

- **Very useful but underutilized embolic agent**
- Sometimes challenging to use
- **However, in many situations, glue is the best choice**
- Familiarity with glue injection is preferable
- Steep learning curve... as with any embolic agent!
- Pay attention to non-target embolization

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SIX PRODUCTS IN A DROP.

ADHESIVE

High tensile strength. Acceptable minimum load is ≥ 435 N [approx. 18 Kgf/cm^2].[2-3]

SEALANT

Applied with dedicated nebulizing devices it forms a thin film with sealing and waterproof properties due to its synthetic nature and strong adhesive power.[3-6]

HAEMOSTATIC

Effective in wet environment.[10]

BACTERIOSTATIC

Blocks bacterial growth for an average of 7 days.[10-12]

SCLEROSANT

Injected into the lumen of a vessel/varices, polymerize generating a plastic cap causing thrombosis and subsequent fibrosis and sclerosis.[13-17]

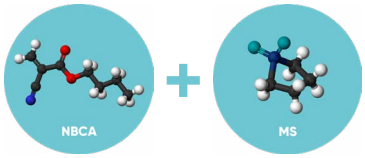
LIQUID EMBOLIZING AGENT[20-81]

Injected into a blood vessel polymerizes building a cast adhers to the vessel occluding it such as an embolus. It causes completely and definitively occlusion without any recanalization, equivalent to surgical ligation.

Tailored dilutions with Ethiodized Oil allow a great modulability of Glubran®2, adaptable to a large variety of cases:

TREATMENTS	GLUBRAN®2/Ethiodized Oil
• Arterial and venous bleeding	1:3-1:6[48,57,58, 84]
• AVM	1:3[84]
• Fistulas	1:1-1:3[24,30,36,46,62,73,79]
• Varicocele	1:1[84]
• Cysts and tumours	1:1-1:6[29,31,67]
• Portal Vein	1:1-1:8[84]
• Endoleaks type II	1:3[41,49,56]

- **Ready to use**
- **Does NOT polymerise in the presence of air**
- **Storage at +2 to +8°C**
- **Can remain at room T (22,5 +/- 2,5°C) per 5 days**



The co-monomer NBCA + MS is an add value to give:

- Polymerisation Temperature: 45°C lower than 80-90 °C typycal of pure monomeric cyanoacrylates like N-Butyl-CyanoAcrylate and Hesyl-Cyanaoacrylate[10-13-61-82]
- NO tissue necrosis[10-12-61-63-64]
- Greater elasticity of the cast at the end of the polymerization[4-6]

Appearance	Odour	Density
TRANSPARENT	TYPICAL OF CYANOACRYLATES	SIMILAR TO WATER

GUIDELINES FOR USING GLUBRAN®2

1. Careful preliminary angiographic examination

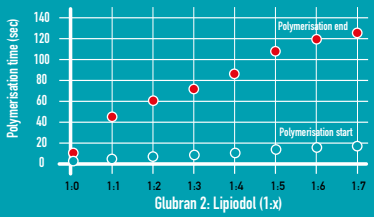
Identification of the afferent and collateral vessels and any eventual AV fistulas, with oblique and cranio-caudal projections

2. Selective and superselective catheterisation of the area to be embolised

3. Careful hemodynamic evaluation

4. Dilute with Lipiodol®:

a) To delay the Glubran®2 to polymerisation start time
b) To make it radiopaque



5. Mix the two compounds uniformly

Immediately before injection (with a 3-way resistant stopcock or in a steel bowl)

6. Wash the catheter with glucose or dextrose solution

7. Inject slowly

- A single injection continuously

- Multi-shot or "sandwich" technique: push the mixture with glucose/dextrose

8. Remove the catheter

(quickly and immediately after the injection, if it was not performed the "sandwich technique" with glucose)

9. Eventual check with contrast medium at least two minutes later

WARNING: DO NOT USE GLUBRAN® 2 WITH POLYCARBONATE OR SILICONE MATERIALS

Advised products & materials

- Glubran® 2/Lipiodol® Ultra-Fluid
- Glucose or dextrose 5%-33%
- Polyethylene (PE) or polypropylene (PP) syringes with luer lock
- 3-way-stopcocks
- Standard 4F catheter
- Coaxial microcatheter

Glubran® 2/Lipiodol® dilution ratios[84]

	MICROCATHETER POSITION	CATHETER TIP	INJECTION OF THE MIXTURE	FLOW SPEED	OCCLUSION	EXAMPLES OF APPLICATIONS
GLUBRAN® 2/LIPIODOL®[84] Dilution ratio 1:1 to 1:3[1-9]	Close to lesion	Wedged	Continuous	High	Proximal	Varicocele, Hypervascularized tumors,Gastro-intestinal bleedings, Peripheral bleedings, Pseudoaneurysms, High-flow AVM
GLUBRAN® 2/LIPIODOL®[84] Dilution ratio 1:4 to 1:9[10-14]	Far from lesion	Free	Drop by drop	Low	Distal	Organ-end artery, Portal vein embolization, Low-flow AVM, Tumor devascularization, Venous malformations, Lymphatic leakage

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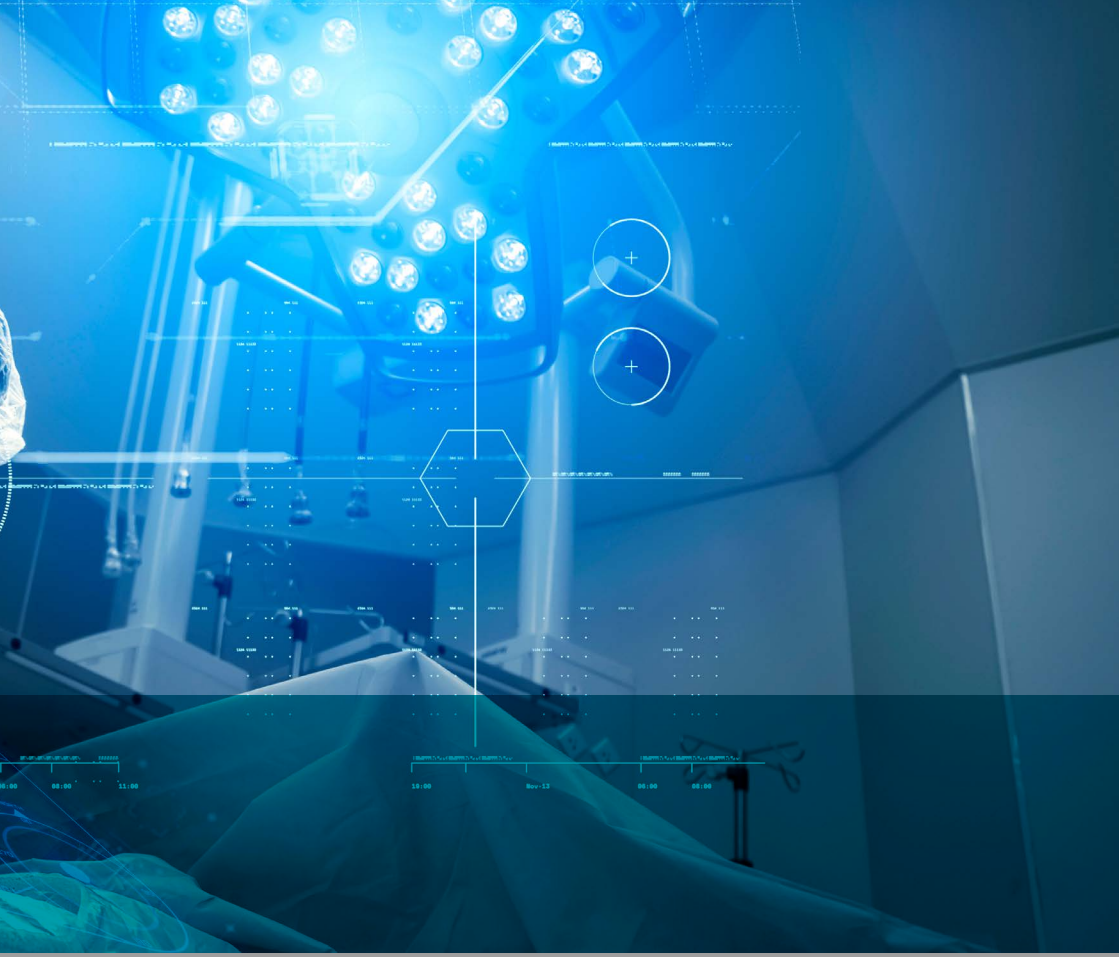

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