The FAIR-Embo Concept: Evolution as an Embolic Agent

Mathieu Di Bisceglie, MD[1]; Gloria Salazar, MD, FSIR[2]; Vincent Vidal, MD, PhD[3]

[1]Assistance Publique – Hopitaux de Marseille, Marseille, France; [2]Department of Radiology, UNC School of Medicine, Chapel Hill, North Carolina; [3]Timone Hospital, Marseille, France

Abstract: Arterial embolization is an interventional radiology technique to occlude a bleeding vessel quickly, efficiently, and safely. It is widely used in Western countries and can often replace surgery to stop childbirth hemorrhage, internal hemorrhage in trauma patients, benign or malignant tumor lesions, and arteriovenous malformations. However, despite its broad clinical indications in many fields, and the fact that embolization has been widely employed in developed countries, it remains unknown and underutilized in many countries around the world, particularly in low-resource settings. In such instances, the lack of availability of this technique is responsible for a significant morbidity and mortality rate, even though it is known to help treat patients and save many lives. Arterial embolization is now the gold standard and first-choice treatment for the management of persistent postpartum bleeding despite well-conducted medical therapy and avoids more invasive procedures such as hysterectomy. In this setting, it is important to have access to readily available interventional teams and equipment to stop hemorrhage by using occluding embolic agents, but unfortunately this does not happen in low- and lower middle-income countries. The FAIR-Embo project supports the use of low-cost embolic materials through an innovative, affordable, and readily available approach that can be employed anywhere in the world.

VASCULAR DISEASE MANAGEMENT. 2022;19(6):E106-E109
Key words: arterial embolization, FAIR-Embo, persistent postpartum bleeding

Introduction

Arterial embolization is an interventional radiology technique to occlude a bleeding vessel quickly, efficiently, and safely.[1] This technique is widely used in Western countries and can often replace surgery to stop childbirth hemorrhage, internal hemorrhage of trauma patients, benign or malignant tumor lesions (uterine fibroids, benign prostatic hypertrophy, hepatic carcinoma), and arteriovenous malformations. Within these procedural categories, there is growing research with continuous development and technical refinements. However, despite its broad clinical indications in many fields, and the fact that embolization has been widely employed in developed countries, it remains unknown and underutilized in many countries around the world, particularly in low-resource settings. In such instances, the lack of availability of this technique is responsible for a significant morbidity and mortality rate, even though it is known to help treat and save many lives. For example, postpartum hemorrhage is the leading cause of maternal mortality in the world, ahead of infections. According to the World Health Organization, approximately 100,000 women die each year from complications of postpartum hemorrhage, and 99% of these deaths occur in developing countries.[2,3,4] Internal hemorrhage from motor vehicle crashes (severe polytrauma) are also responsible for a high mortality rate in emerging countries.[5] Arterial embolization is now the gold standard and first-choice treatment for the management of persistent postpartum bleeding despite well-conducted medical therapy and avoids more invasive procedures such as hysterectomy. In this setting, it is important to have access to readily available interventional teams and equipment to stop hemorrhage by using occluding embolic agents, but unfortunately this does not happen in low- and lower middle-income countries. The FAIR-Embo project supports the use of low-cost embolic materials through an innovative, affordable, and readily available approach that can be employed anywhere in the world.

The Project

In 2018, the FAIR-Embo project was started following a simple and implacable observation: Even though low-resource countries have the workforce (interventional radiologists) and equipment (angiography tables), hospitals still do not have access to currently available embolization agents needed to establish an interventional radiology (IR) service focused on embolization procedures. This is particularly true in Dakar, Senegal, where trained radiologists (professors Ababacar Mbengue and Abdoulaye Ndoye Diop) often lack the "consumable" equipment, including embolization agents, needed to perform optimal IR. Two main reasons are given: In addition to the price of embolization agents, the lack of a distribution network for medical equipment, particularly for these agents, hinders the use of arterial embolization procedures. This lack of availability of embolization agents in many countries has led to the idea of developing a product that would be available at any time in any hospital in the world, easy to use, with a similar safety and effectiveness profile to current embolic agents on the market to perform an adequate embolization procedure.

The Agent: Use of Sutures

The use of silk sutures (surgical sutures used before the advent of synthetic sutures) or small fragments of sterile compresses have already been tested in the past, but their respective properties were responsible for inflammatory granuloma and endovascular enclavement during embolization procedures.[1]

However, synthetic sutures are consumable medical materials used worldwide and available in almost every hospital, especially in low-resource countries. They are also inexpensive compared with the embolization agents currently used. While their use for arterial embolization procedures has never been studied before, they are widely used in endovascular surgical procedures, such as vessel/organ sutures in vascular or cardiac surgery. In addition, some types of sutures are based on nylon, a material used in the manufacture of fibrous coils used in current embolization procedures for its well-studied thrombogenic property.[6]

With respect to biocompatibility, sutures are considered class III medical devices and meet the health and safety requirements for this type of medical material. In accordance with the Public Health Code (European Directive 93/42/EEC on medical devices), the suture components and their degradation products meet specific criteria concerning their biological safety: in vitro cytotoxicity and sensitization; in vivo irritation; biological reaction; acute, systemic, and chronic toxicities; genotoxicity; carcinogenicity; teratogenicity; hemocompatibility; pyrogenicity; and antigenicity. As sutures are used in vascular and cardiac procedures, they are in contact with blood elements in the same way as during embolization, thus supporting their biocompatible nature in this use.

Synthetic sutures therefore appear to be "potential" embolization agents that are available, inexpensive, and safe from a biocompatibility point of view.

Preclinical Studies and Translation to Clinical Applications

FAIR-Embo's inaugural study was published in 2019,[7] where the suture-embolic applicability in occluding vessels was demonstrated for the first time, injecting a suture fragment (1- to 2-cm long) via a 5 Fr catheter, with subsequent vascular occlusion in a target artery of a porcine model (**Figure 1**). The histological analysis post embolization did not demonstrate inflammatory changes at the organ embolized in the short- and medium-term follow-up (up to 3 months). These initial results, achieved with both absorbable (Vicryl braided suture, Ethicon) and nonabsorbable sutures (Mersutures, Ethicon), were instrumental to proceed with the evaluation of a more definitive or transient embolization endpoint, leading to subsequent development of the FAIR-Embo project.

A second preclinical study, published in October 2020[8], demonstrated that homemade suture-based microparticles made from nylon Flexocrin wire (B. Braun) had comparable efficacy to Embozene 900 microspheres (Varian) for distal renal artery embolization (**Figure 2**). There were no significant complications compared with the control group, either in the short term

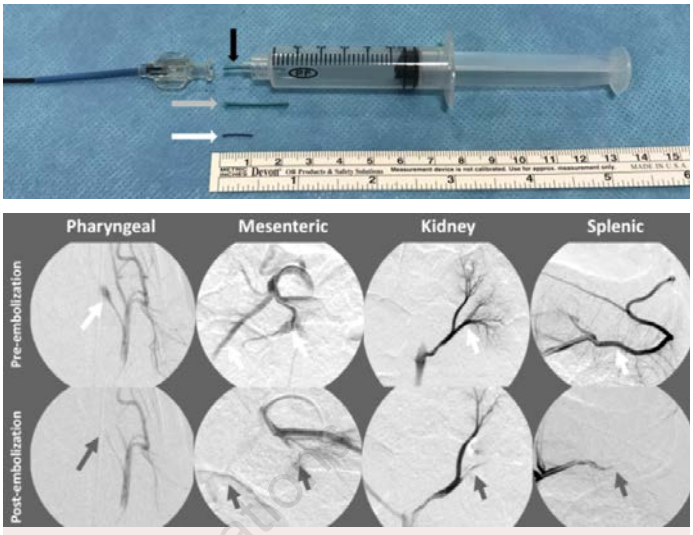

Figure 1. First preclinical study: proximal arterial embolization with suture fragments (1- to 2-cm long). Embolization was effective in every artery studied.

(no increase in off-target embolization) or the medium term (no significant inflammatory changes on histological controls performed). The main difference between the use of microparticles made from sutures and the microspheres was the time duration of the intervention necessary to obtain an effective embolization, caused by a lack of suspension of microparticles in saline or iodine medium, but also because of the noncalibration of the particles, such as noncalibrated polyvinyl alcohol (PVA) particles. These observations led to the next endpoints of the research with the goal of improving the optimal use of this new embolization agent.

Following the preclinical studies performed and published in 2019 and then 2020, local teams have been performing arterial embolization procedures using suture fragments. In early 2020, Professor A.N. Diop's team at Dakar University Hospital in Senegal embolized a postrenal biopsy renal artery pseudoaneurysm in a 29-year-old female patient with anemia (**Figure 3**). The embolization by FAIR-Embo method used Damacryl absorbable wire (GMD Group) in a 20-mm fragment shape. The embolization was effective, with control of the bleeding, and the various controls carried out since then did not show any arterial recanalization or remote complications (including absence of infectious complications). This first FAIR-Embo case was published in April 2020[9] by the Senegalese radiology team, which reminded us of the importance of arterial embolization and, more globally, of IR as a public health tool in multiple disease processes in countries with a low level of development (the necessary equipment: an angiography arch, a catheter, and sutures), and of the importance of this project in the expansion of this specialty throughout the world.

Since this case was published, other patients have been treated by the FAIR-Embo method, whether in Senegal following the example described above, or in Algeria by Dr. Habouchi's team, who recently presented, at the international congress PAIRS, cases of patients with postpartum bleeding treated by the FAIR-Embo method.

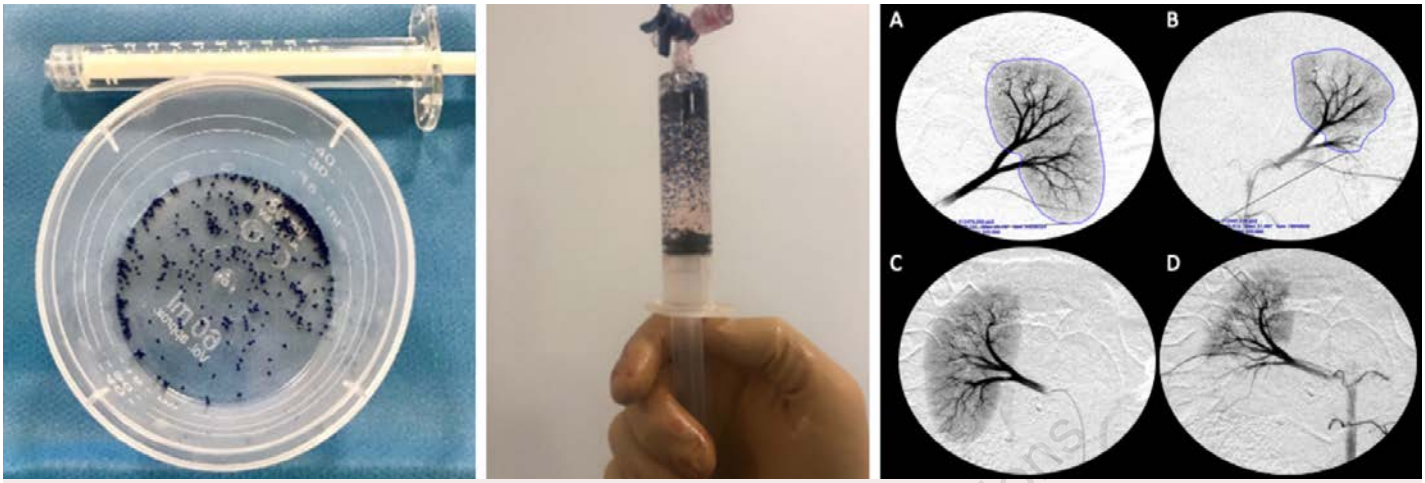

Figure 2. Second preclinical study: renal embolization with suture-based microparticles (**A**,**B**) compared with Embozene 900 (Verian) (**C**,**D**).

Technical Improvements

Certain difficulties appeared during the preclinical study concerning the injection of microparticles made from sutures. The components of the sutures tested, as well as the nonspherical shape of the microparticles produced using hospital scissors, causes an aggregation effect of the microparticles between them and a defect of passage within the catheter in the saline and iodine medium usually used. This results in difficulty of injection compared with usual embolization agents (eg, calibrated microspheres), leading to an increase in the number of injections and therefore a longer procedure time to obtain an effective embolization (occlusion of the target artery). The preclinical study thus shows a significant increase in the time required for embolization compared to the Embozene microparticles used in the control group.[8]

Two main areas of improvement of the microparticles seem essential. First, the ability to inject these microparticles easily and rapidly could be improved by modifying the differences in surfactant activity between the microparticles and the injection solution medium. On the other hand, having a predefined and regular size for the microparticles would make it possible to establish precise indications for the use of these calibrated microparticles, similar to the different sizes used for microspheres currently on the market (eg, use of 700 µm microparticles for the treatment of uterine fibroids). The calibration of microparticles on precise threshold values is essential to guarantee both the effectiveness and safety of the technique when using microparticles. A suture cutting tool is currently being developed in collaboration with an engineering school. The tool should be easy to use, inexpensive, and reliable over time, allowing for faster and more accurate microparticle fabrication compared with the manual method of hospital scissors currently used. This will have a major impact on the acceptance of the use of this type of agent as an embolization product in specific indications.

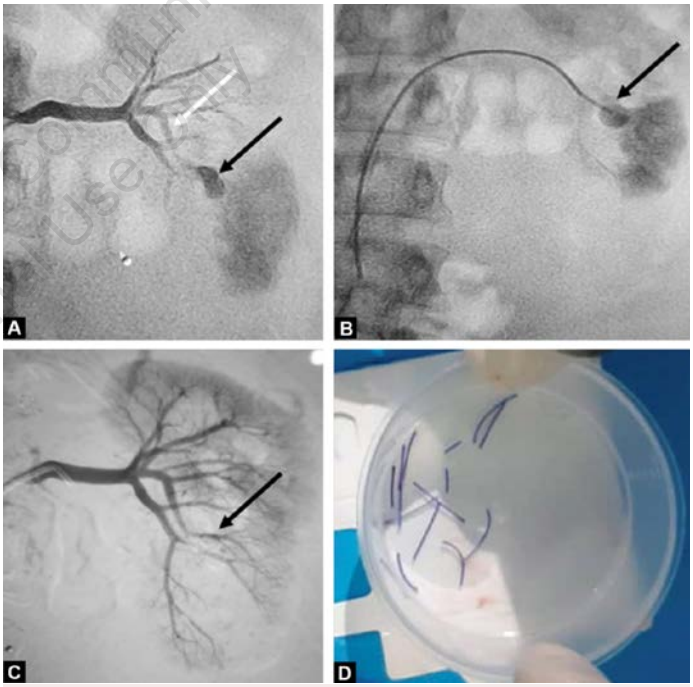

Figure 3. First FAIR-Embo case report: embolization of a pseudoaneurysm of the left renal artery by 2-cm suture fragments.

Conclusion

The project is already international; rapidly expanding clinical development and an overall objective of developing IR as a valuable tool in the treatment of multiple pathologies in countries without access to affordable and available treatment techniques seems ambitious, but realistic. The FAIR-Embo project combines international skills from France, the United States, Canada, Senegal, Togo, Ivory Coast, Cameroon, Chad, Mauritania, Algeria, and Cambodia, proposing a real consortium with the will to promote this discipline.

The development of the FAIR-Embo technique alone would not be able to alleviate all the difficulties of access to this type of treatment in developing countries. Indeed, how can one imagine arterial embolization with suture fragments in hospitals that do not have an adequate angiography table, embolization equipment, or trained radiologists?

The FAIR-Embo project has a global goal in its objective to provide access to IR care in low-development countries. A FAIR-Embo chair within the Aix Marseille University Foundation was created in 2020, with the aim of raising funds with 2 main objectives: to help distribute equipment and to train local radiologists through partnerships and local missions.

IR is an extremely diverse specialty and could allow, through a single trained radiologist, for the management of many urgent situations: hemorrhages related to road accidents, maternal hemorrhages, and certain neoplastic lesions. Sometimes considered an "elite" specialty highly dependent on technological advances, it is also a field based on innovation, creativity, and vision, which has the potential to treat patients in an innovative and minimally invasive way, safely and effectively. As such, it has much to offer to global health, starting now. Many procedures can be performed using relatively inexpensive and available imaging modalities. The misconception that this specialty belongs only to wealthy nations must be replaced with creativity to find solutions in developing countries. With the help of international humanitarian organizations, and by adapting traditional approaches to basic procedural techniques with local means such as the FAIR-Embo project, radiologists can make a significant contribution to the global community. ■

Disclosure: The authors have completed and returned the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors report no conflicts of interest regarding the content herein.

Manuscript accepted May 25, 2022.

Address for correspondence: Vincent Vidal, MD, Timone Hospital, 264 Rue Saint-Pierre, 13005 Marseille, France. Email: Vincent.Vidal@ap-hm.fr

REFERENCES

1. Baum RA, Baum S. Interventional radiology: a half century of innovation. *Radiology*. 2014;273(2 Suppl):S75-S91. doi:10.1148/radiol.14140534
2. Makris GC, Byrne G. Post-partum hemorrhage and maternal mortality in low-income countries and the forgotten role of interventional radiology. *Cardiovasc Intervent Radiol*. 2019;42(12):1810-1811. doi:10.1007/s00270-019-02339-x
3. Say L, Chou D, Gemmill A, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014;2(6):e323-e333. doi:10.1016/S2214-109X(14)70227-X
4. Sobhy S, Arroyo-Manzano D, Murugesu N, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet*. 2019;393(10184):1973-1982. doi:10.1016/S0140-6736(18)32386-9
5. Sakran JV, Greer SE, Werlin E, McCunn M. Care of the injured worldwide: trauma still the neglected disease of modern society. *Scand J Trauma Resusc Emerg Med*. 2012;20:64. doi:10.1186/1757-7241-20-64
6. Trerotola SO, Pressler GA, Premanandan C. Nylon fibered versus non-fibered embolization coils: comparison in a swine model. *J Vasc Interv Radiol*. 2019;30(6):949-955. doi:10.1016/j.jvir.2018.10.004
7. Vidal V, Hak JF, Brige P, et al. In vivo feasibility of arterial embolization with permanent and absorbable suture: the FAIR-Embo concept. *Cardiovasc Intervent Radiol*. 2019;42(8):1175-1182. doi:10.1007/s00270-019-02211-y
8. Di Bisceglie M, Hak J-F, Diop AD, et al. FairEmbo concept for arterial embolizations: in vivo feasibility and safety study with suture-based microparticles compared with microspheres. *Cardiovasc Intervent Radiol*. 2021;44(4):625-632. doi: 10.1007/s00270-020-02678-0
9. Diop AD, Diop AN, Hak JF, et al. Hemostatic embolization of renal artery pseudoaneurysm using absorbable surgical suture (FairEmbo concept). *Diagn Interv Imaging*. 2020;101(11):757-758. doi:10.1016/j.diii.2020.04.002