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TECHNICAL NOTE

Pulmonary Arteriovenous Malformations Embolized Using a Micro Vascular Plug System: Technical Note on a Preliminary Experience

Emanuele Boatta[1] · Christine Jahn[1] · Matthieu Canuet[2] · Julien Garnon[1] · Nitin Ramamurthy[3] · Roberto Luigi Cazzato[1] · Afshin Gangi[1]

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Abstract
AIM To report our preliminary experience using a Micro Vascular Plug (MVP) deployed through a 2.8Fr microcatheter for the treatment of pulmonary arteriovenous malformations (PAVMs) in a cohort of patients affected by Hereditary Haemorrhagic Telangiectasia (HHT).
Materials and Methods Four consecutive female patients (mean age 38.0 years; range 25–55 years) with PAVMs diagnosed on echocardiogram/bubble test and contrast-enhanced CT (CECT) underwent MVP embolization. One patient was symptomatic with recent transient ischaemic attack. Follow-up was undertaken at 1-month post-procedure with CECT to assess PAVMs permeability and MVP positioning and at 1-, 6-, and 12-month post-procedure, with echocardiography/bubble test and standard neurological history, to confirm absence of right-to-left shunts and recurrent symptoms.
Results Eight PAVMs were treated in 4 patients over 5 interventional sessions (mean 1.6 PAVMs per session). All PAVMs were simple, with mean feeding artery diameter of 4.25 mm. Eight 6.5 mm MVPs were deployed in total (one per lesion). Technical success was 100%. Mean procedural time and patient dose per session were 70 min (range 40–70 min) and 53418 mGy.cm^2 (range 6113–101628 mGy.cm^2), respectively. No signs of reperfusion neither of MPV migration were noted at 1-month CECT follow-up. At early follow-up (mean 3.75 months; range 1–12 months), clinical success was 100% with no evidence of recurrent right-to-left shunt, and no neurological symptoms. No immediate or late complications were observed.
Conclusions MVP embolization of PAVMs appears technically feasible, safe, and effective at early follow-up. Further prospective studies are required to confirm long-term safety and efficacy of this promising technique.

Keywords Hereditary hemorrhagic telangiectasia · Pulmonary arteriovenous malformations · Embolization · Micro-Vascular Plug

The original version of this article was revised: In the original article the name of the first author was misspelled as "Eanuele Boatta". The correct spelling is "Emanuele Boatta".

✉ Roberto Luigi Cazzato
gigicazzato@hotmail.it

Emanuele Boatta
emanuele.boatta@yahoo.it

Christine Jahn
christine.jahn@chru-strasbourg.fr

Matthieu Canuet
matthieu.canuet@chru-strasbourg.fr

Julien Garnon
juleiengarnon@gmail.com

Nitin Ramamurthy
nitin_ramamurthy@hotmail.com

Afshin Gangi
gangi@unistra.fr

[1] Service de Imagerie Interventionelle, Nouvel Hôpital Civil, Hôpitaux Universitaires de Strasbourg, Place de l'Hôpital, 67000 Strasbourg, France

[2] Service Service de Pneumologie, Nouvel Hôpital Civil, Hôpitaux Universitaires de Strasbourg, Place de l'Hôpital, 67000 Strasbourg, France

[3] Department of Radiology, Norfolk and Norwich University Hospital, Colney Lane, Norwich NR4 7UY, UK

Introduction

Pulmonary arteriovenous malformations (PAVMs) are uncommon lesions characterized by anomalous communications between pulmonary arteries and veins; 80% occur in association with Hereditary Haemorrhagic Telangiectasia (HHT), a rare autosomal dominant disorder in which small-vessel dysplasia predisposes to recurrent epistaxis, muco-cutaneous telangiectasia, and visceral AVMs [1, 2]. PAVMs bypass pulmonary capillaries and form a right-to-left shunt, resulting in complications including haemorrhage, cyanosis, and paradoxical emboli (e.g. stroke, cerebral abscess) [3, 4]. Treatment is imperative to avoid morbidity.

Endovascular embolization is the treatment of choice, and has been shown to ameliorate symptoms and prevent complications [5]. Anatomically, PAVMs comprise one or more feeding arteries, an aneurysmal sac (or dilated vascular plexus), and one or more draining veins; 80% are "simple" (single feeding artery); the remainder are "complex" (multiple/multilobar vessels) [1]. The aim of treatment is to selectively occlude distally the feeding vessel(s) as close as possible to the sac, and to avoid systemic device migration. Several devices have been employed including various coils [6–11], micro-coils [12], and vascular plugs [13–15]—with plugs increasingly preferred [14]. However, even the latest generation may be unsuitable for small lesions with tortuous feeding vessels [16], and alternatives have been sought.

Micro Vascular Plugs (MVPs) represent a novel detachable, re-sheathable embolic device composed of a self-expanding nitinol cage partially covered by a polytetrafluoroethylene (PTFE) membrane [17]. The design enables controlled deployment/repositioning, rapid vascular occlusion, and compatibility with standard micro-catheters for easy navigability within tiny, tortuous vessels [18]. Early reports have demonstrated good technical feasibility and short-term efficacy in the abdominal and cerebral circulation, and a recent report has successfully applied the technique to PAVMs [17–20].

The aim of this study is to present our preliminary experience of MVP embolization of PAVMs, and discuss technical aspects, advantages, and limitations of this novel technique.

Materials and Methods

Study Population

This retrospective study was undertaken with the Institutional Review Board approval.

Review of electronic records identified four consecutive female patients (mean age 38.0 ± 12.7 years; range 25–55 years; Table 1) affected by HHT and treated for one or more PAVMs between February 2015 and June 2016. One patient was symptomatic with recent transient ischaemic attack (temporary, self-limiting right hemiparesis); the remainder was asymptomatic. Patients were referred for embolization following discussion between the attending pulmonologist and treating interventional radiologist, in order to prevent future cerebrovascular accidents. All PAVMs were confirmed on echocardiography/bubble test showing right-to-left shunts and using contrast-enhanced computed tomography (CECT) in order to localize lesions and assess the number/size of feeding arteries and draining veins.

PAVM Embolization Procedure

All procedures were performed in an angiographic room equipped with a flat-panel C-arm Cone Beam CT system (Philips Healthcare, the Netherlands). XperCT and Embo-Guide tools (Philips Healthcare, the Netherlands) were available in the angiographic unit.

For bilateral PAVMs, staged embolization was performed by treating one side per session to minimize the risk of bilateral post-embolization chest pain/pleural effusion.

Anticoagulants were stopped 5 days prior, and blood clotting parameters were tested 24 h pre-procedure, ensuring minimum prothrombin time of 50% and platelet count of 50000/mm^3 according to the Society of Interventional Radiology (SIR) guidelines [21]. Antibiotic prophylaxis was administered prior to the procedure and 5000UI heparin was administered i.v. intra-procedurally.

The right femoral vein was cannulated using a 6Fr Super Sheath introducer (Boston Scientific, Marlborough, MA, USA), and a 4Fr Imager TM II pig-tail catheter (Boston Scientific, Marlborough, MA, USA) was advanced into the target main pulmonary artery. Pulmonary angiography with 3D rotational acquisition was performed 5 s following the injection of 40 ml of contrast at 8 ml/s. Data were post-processed using Embo-Guide software (Philips Healthcare, Best, the Netherlands) to confirm presence of PAVMs, automatically delineate the feeding arteries, and generate a continuous 3D Road-Map to optimize endovascular navigation and reduce contrast administration, procedural time, and radiation exposure [22].

A 6Fr Neuron catheter (Penumbra Inc, Alameda, California, USA) was then exchanged over the guidewire and advanced (with continuous heparinated saline flushing—2500UI/1000 ml saline—through a Y connector to avoid clots formation inside the catheter and to reduce the risk of neurological complications) to the level of the target pulmonary artery branch, in order to improve stability for selective catheterisation.

A 2.8 Fr Progreat micro-catheter (Terumo Corporation, Tokyo, Japan; inner diameter 0.027″) was co-axially positioned as distally as possible within the feeding artery; an MVP-5 delivery system (Reverse Medical Corporation, Irvine, CA, USA) was advanced and unsheathed to occlude

Table 1 Population and procedural data

	Patients	Sex, age	N. of treated PAVMs	Pulmonary Lobe	Feeding artery (mm)	Draining vein (mm)	Plug size (mm)	Technical success	Follow-up (months)
	1	F, 25	1	RI	4	6	6.5	Yes	1
	2	F, 33	1	LS	5	7	6.5	Yes	3
	3	F, 39	4	RI	4	7	6.5	Yes	12
				RS	3	6	6.5	Yes	
				RI	3	6	6.5	Yes	
				LI	5	7	6.5	Yes	
				LI	5	7	6.5	Yes	
	4	F, 55	1	RS	5	7	6.5	Yes	1
Mean (SD)		38.0 (12.7)			4.25 (0.9)	6.6 (0.5)			3.75 (4.8)

RI right inferior, *LS* left superior, *RS* right superior, *LI* left inferior

the target vessel (i.e. feeding artery). Selective angiogram was performed using 1 ml of contrast injected via a Y connector, to confirm vascular occlusion. The MVP was then deployed using the proprietary detachment system; and a final angiogram was obtained after 3–4 min to confirm satisfactory position and feeding artery occlusion (Fig. 1).

Following the procedure, patients were admitted to a recovery ward for observation and discharged after 24-h when medically fit.

Follow-up

All patients underwent clinical review by the treating interventional radiologist, and echocardiography with bubble test, at 1-, 6-, and 12-month post-procedure in order to assess clinical evolution (neurological symptoms assessed using standard neurological history), and confirm absence of right-to-left shunts.

CECT was obtained 1-month post-procedure to rule out MPV migration distally from the feeding artery and to assess PAVMs occlusion.

Data collection and analysis

Demographics, number/location of PAVMs, size of feeding arteries and draining vein (axial diameter on pre-procedural CECT), procedural time (between initial and final angiograms), patient dose (dose area product—DAP-calculated

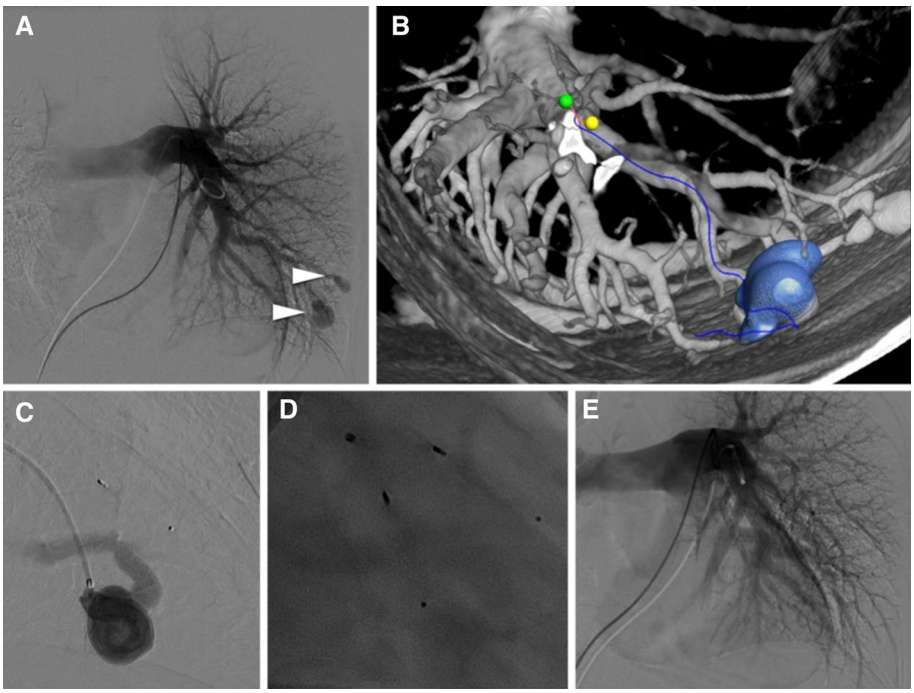

Fig. 1 **A** Angiogram showing 2 PAVMs in the anterobasal segment of the *left* inferior lung lobe with feeding arteries measuring 3 and 3.5 mm (*arrowheads*), respectively. **B** Embo-Guide post-processing images automatically depicting the feeding artery (*blue line*) of one of the two PAVMs (*blue ball*). **C** Selective angiography of one of the two PAVMs performed via the 2.8Fr microcatheter. **D** Two MVP devices in the feeding arteries (one for each artery/PAVM). **E** Final angiography after embolization obtained from the main left pulmonary artery shows complete occlusion of both PAVMs

using proprietary angiographic software), technical success and complications, and clinical outcomes were evaluated using retrospective chart review.

Technical success was defined as accurate selective and distal (<1 cm from PAVM sac) MVP deployment in the feeding artery, with complete devascularisation of the aneurysmal sac and draining vein on final angiogram.

Complications were classified according to the SIR grading system [21].

Clinical success was defined as absence of clinical symptoms and echocardiographic right-to-left shunt at last available follow-up.

In the end, at 1-month CECT follow-up, complete PAVMs occlusion was granted when no CE was noted in the draining vein; at the same time, MPV migration was granted if the MPV moved distally from the feeding artery.

Results

Eight PAVMs were treated in 4 patients over 5 interventional sessions (mean 1.6 PAVMs per session). One patient presented with 5 PAVMs requiring two therapeutic sessions (one for each side). All PAVMs were simple, with a single feeding artery and draining vein. Lesions were located in the right inferior (37.5%), left inferior (25%), right superior (25%), and left superior (12.5%) lobes. Mean diameter of feeding arteries was 4.25 mm. A single 6.5 mm (unconstrained diameter) MVP was deployed in each case (8 in total; Table 1).

Technical success was 100%, with satisfactory MVP position and complete devascularisation of all PAVMs on final angiography. No cases required MVP repositioning, or placement of multiple devices. Mean procedural time and patient dose per session were 70 ± 18.7 min (range 40–70 min) and 53418 ± 40211 mGy.cm^2 (range 6113–101628 mGy.cm^2), respectively.

One-month CECT follow-up revealed complete PAVMs devascularisation and absence of MPV migration in all cases.

At early follow-up (mean 3.75 months; range 1–12 months), clinical success was 100% with no evidence of right-to-left shunt on echocardiograms, and no neurological symptoms. No immediate or late complications were observed.

Discussion

Endovascular therapy of high-flow PAVMs presents significant challenges due to the high risk of device migration; the need for precise positioning close to the aneurysmal sac to avoid non-target embolization and late recanalization [23] and difficult access via diminutive, tortuous feeding vessels [16]. It is imperative to select an appropriate embolic device based on anatomy (feeding artery diameter, landing-zone length, and tortuosity of access), technical ease, and long-term outcomes.

Historically, pushable steel coils were initially used with good vascular occlusion. However, there was a significant risk of migration, non-target vessel occlusion, and delayed recanalization [6–9]. The introduction of the Amplatzer Vascular Plug (AVP) and detachable/interlocking coils made the procedure safer and easier, enabling precise placement/repositioning, and a lower risk of migration [9–11, 14–16, 24, 25]. In particular, AVPs have offered procedural simplicity with deployment of a single device, and good long-term outcomes with recanalization rates of only 5–7% (particularly when "backed-up" with coils) [9, 13, 15, 16, 24, 25]. Latest-generation devices have further improved accessibility of remote lesions: the AVP-IV (4Fr, inner diameter 0.038 inches) is navigable for the majority of lesions; the development of 0.018 inch coils delivered through 3–4 Fr micro-catheters has enabled access to more remote, tortuous feeding vessels [12].

Nevertheless, both coils and AVPs present limitations. Coiling typically requires multiple devices, and often, longer procedure times. There remains a small risk of migration [10, 13], and reported recanalization rates were higher than AVPs (4 vs. 19%) [5, 9, 16] including at long-term follow-up (37 PAVMs embolized with coils, 21 with AVPs type I, II, and IV; median follow-up 7.8 and 6.9 years in the coil and AVP group, respectively) [14], although definitive proves are lacking. Some authors applied a combined technique (AVP plus coiling) in order to reduce the recanalization rate of the feeding artery [15]; we did not use such technique since the MPV is a partially PTFE-covered device. AVPs require a rigid delivery system and even the AVP-IV may be unsuitable for small, tortuous feeding vessels. Finally, both devices are clotting-based, and the risk of distal embolization cannot be ruled out completely [9].

Micro Vascular Plugs (MVPs) appear to combine the efficacy of AVPs with the navigability of micro-coils. The controllable mechanical detachment system enables precise placement/repositioning; "check angiography" may be performed pre-deployment to assess effects on vascular flow [19], which should stop immediately after MPV positioning in the vessel before deployment, since it is a partially covered device. If blood flow does not immediately stop, this means that the size of the device is underestimated compared to the diameter of the target vessel; therefore, a potential migration may occur if the device is deployed. In this case, the device must be retracted and exchanged with a bigger one. During such process, blood clotting and distal embolization may theoretically occur; however, such risk is theoretical and

may occur also with other occluding devices (e.g. coils, AVP). Accordingly, any kind of device repositioning must be avoided and, precise vessel sizing is mandatory on pre-procedural imaging in order to select the best fitting device, including MPVs.

The design offers intrinsic radial force, is suitable for short landing zones, and only one device is usually required [17]. It is recommended for 1.5–5 mm vessels, and is delivered through a standard micro-catheter over a 0.018 nitinol wire, allowing distal embolization in remote, tortuous vessels [19]. Finally, the PTFE coating facilitates mechanical occlusion, minimizing risk of clot embolization [18].

To our knowledge, only Conrad et al. have utilized MPVs for PAVMs [20]. In a recent report of 7 cases with 20 PAVMs, authors successfully placed 21/23 MVPs with immediate cessation of flow [20] and no significant early complications. However, there was one case of delayed device migration at 3 months, possibly due to a relatively under-sized plug [26]. To our knowledge, there are no reports of this technique in the European literature.

We utilized 8 MVPs to treat 8 PAVMs in 4 HHT patients with tortuous pulmonary vascular anatomy, with 100% technical success and no immediate complications. Procedures were rapid and relatively easy, and we positioned devices close to the aneurysmal sac with high confidence, thanks to the precise deployment system and ability to perform pre-deployment angiography. At short-term follow-up (mean 3.75 mo), clinical success was 100%, with no recurrent neurological symptoms and normal echocardiogram/bubble test. Moreover, at 1-month CECT, no signs of MPV migration were noted in all cases. Our results appear promising, corroborate the previous study [20], and add to the emerging literature supporting this novel technique.

Limitations include retrospective design and the small sample of simple PAVMS only, limiting generalizability. We did not perform long-term CT follow-up, limiting anatomic assessment of migration and therapeutic success [7]. However, echocardiogram/bubble test has high sensitivity and negative predictive value [4] and excludes clinically significant treatment failure. Respiratory status was not formally assessed because patients were either asymptomatic or had previous neurological events; therefore only neurological symptoms were reviewed. Moreover, our follow-up period has short- and long-term risk of migration and recanalization has not been assessed. In particular, although MPV is a partially PTFE-covered device thus reducing the risk of recanalization, confirmation with long-term data is mandatory to prove this aspect.

Finally, our follow-up was obtained with CECT even though recent advances enable radiation- and contrast-free imaging of PAVMs with MRI [27, 28]; this point may be particularly useful in patients affected by HTT and PAVMs due to their young age.

In conclusion, MVP embolization of PAVMs appears technically feasible, simple to perform, safe, and effective at early follow-up. The device may combine the safety and efficacy of vascular plugs with the manoeuvrability of coils, and could represent the future device of choice for challenging PAVMs. Further prospective studies are required to confirm the long-term safety and efficacy of this novel and promising technique.

Complianve with Ethical Standards

Conflict of interest The authors declared that they have no conflict of interest to disclose.

Ethical Approval For this type of study formal consent is not required.

Human and Animal Rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

References

1. Lacombe P, Lacout A, Marcy P, et al. Diagnosis and treatment of pulmonary arteriovenous malformations in hereditary hemorrhagic telangiectasia: an overview. Diagn Interv Imaging. 2013;94:835–48.
2. Kjeldsen AD, Vase P, Green A. Hereditary haemorrhagic telangiectasia: a population based study of prevalence and mortality in Danish patients. J Intern Med. 1999;245:31–9.
3. Cottin V, Plauchu H, Bayle JY, et al. Pulmonary arteriovenous malformations in patients with hereditary haemorrhagic telangectasia. Am J Respir Crit Care Med. 2004;169:994–1000.
4. Cartin-Ceba R, Swanson KL, Krowka MJ. Pulmonary arteriovenous malformations. Chest. 2013;144(3):1033–44.
5. Faughnan ME, Palda VA, Garcia-Tsao G, et al. International Guidelines for the Diagnosis and Management of Hereditary Haemorrhagic Telangiectasia. J Med Genet. 2011;48:73–87.
6. Remy-Jardin M, Wattinne L, Remy J. Transcatheter occlusion of pulmonary arterial circulation and collateral supply: failures, incidents, and complications. Radiology. 1991;180:699–705.
7. Remy-Jardin M, Dumont P, Brillet PY, Dupuis P, Duhamel A, Remy J. Pulmonary arteriovenous malformations treated with embolotherapy: helical CT evaluation of long-term effectiveness after 2–21-year follow-up. Radiology. 2006;239:576–85.
8. Pollak JS, Saluja S, Thabet A, Henderson KJ, Denbow N, White RI Jr. Clinical and anatomic outcomes after embolotherapy of pulmonary arteriovenous malformations. J Vasc Interv Radiol. 2006;17:35–44.
9. Letourneau-Guillon L, Faughnan ME, Soulez G, et al. Embolization of pulmonary arteriovenous malformation with amplatzer vascular plugs: safety and midterm effectiveness. J Vasc Interv Radiol. 2010;21(5):649–56.

10. Funaki B. Embolization of pulmonary arteriovenous malformations. Semin Interv Radiol. 2007;24(3):350–5.
11. Shimizu K, Yamazoe S, Ouchi K, Mogami T, Harada J. Embolotherapy of Pulmonary Arteriovenous Malformation Using Detachable Coils. Jikeikai Med J. 2012;59:37–43.
12. Dinkel HP, Triller J. Pulmonary arteriovenous malformations: embolotherapy with superselective coaxial catheter placement and filling of venous sac with Guglielmi detachable coils. Radiology. 2002;223:709–14.
13. Abdel Aal AK, Ibrahim RM, Moustafa AS, Hamed MF, Saddekni S. Persistence of pulmonary arteriovenous malformations after successful embolotherapy with Amplatzer vascular plug: long-term results. Diagn Interv Radiol. 2016;22(4):358–64.
14. Tau N, Atar E, Mei-Zahav M, Bachar GN, Dagan T, Birk E. Bruckheimer E6. Amplatzer Vascular Plugs versus coils for embolization of pulmonary arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia. Cardiovasc Intervent Radiol. 2016;39(8):1110–4.
15. Trerotola S, Pyeritz R. Does Use of coils in addition to Amplatzer vascular Plugs prevent recanalisation? Am J Roentgenol. 2010;195(3):766–71.
16. Trerotola SO, Pyeritz RE. PAVM embolization: an update. AJR Am J Roentgenol. 2010;195(4):837–45.
17. Pellerin O, Maleux G, Déan C, Pernot S, Golzarian J, Sapoval M. Microvascular plug: a new embolic material for hepatic arterial skeletonization. Cardiovasc Interv Radiol. 2014;37(6):1597–601.
18. Shwe Y, Paramasivam S, Ortega-Gutierrez S, Altschul D, Berenstein A, Fifi JT. High-flow carotid cavernous fistula and the use of a microvascular plug system: initial experience. Interv Neurol. 2015;3(2):78–84.
19. Hao F, Powell D, Weintraub J, Sheynzon V. Pediatric Gastroduodenal Embolization with a Microvascular Plug. Cardiovasc Interv Radiol. 2016;39(5):788–90.
20. Conrad MB, Ishaque BM, Surman AM, Kerlan RK Jr, Hope MD, Dickey MA, Hetts SW, Wilson MW. Intraprocedural safety and technical success of the MVP Micro Vascular Plug for embolization of pulmonary arteriovenous malformations. J Vasc Interv Radiol. 2015;26(11):1735–9.
21. Sacks D, McClenny TE, Cardella JF, Lewis CA. Society of Interventional Radiology clinical practice guidelines. J Vasc Interv Radiol. 2003;14:S199–202.
22. Tacher V, Radaelli A, Lin M, Geschwind JF. How I do it: cone-beam CT during transarterial chemoembolization for liver cancer. Radiology. 2015;274(2):320–34.
23. Milic A, Chan RP, Cohen JH, Faughnan ME. Reperfusion of pulmonary arteriovenous malformations after embolotherapy. J Vasc Interv Radiol. 2005;16:1675–83.
24. Tapping CR, Ettles DF, Robinson GJ, et al. Long-term follow-up of treatment of pulmonary arteriovenous malformations with Amplatzer vascular Plugs and Amplatzer vascular plugs II devices. J Vasc Interv Radiol. 2011;22(12):1740–6.
25. Hart J, Aldin Z, Braude P, Shovlin C, Jackson J. Embolization of pulmonary arteriovenous malformations using the Amplatzer vascular plug: successful treatment of 69 consecutive patients. Eur Radiol. 2010;20:2663–70.
26. Microvascular plugs investigated in embolization of pulmonary arteriovenous malformations. Interventional News. Monday, 30 Nov 2015. http://www.cxvascular.com/in-features/interventional-news—features/microvascular-plugs-investigated-in-embolization-of-pulmonary-arteriovenous-malformations. Accessed 20 July 2016.
27. Hamamoto K, Matsuura K, Chiba E, Okochi T, Tanno K, Tanaka O. Feasibility of non-contrast-enhanced mr angiography using the time-slip technique for the assessment of pulmonary arteriovenous malformation. Magn Resonance Med Sci. 2016;15(3):253–65.
28. Schneider G, Uder M, Koehler M, Kirchin MA, Massmann A, Buecker A, Geisthoff U. MR angiography for detection of pulmonary arteriovenous malformations in patients with hereditary hemorrhagic telangiectasia. AJR Am J Roentgenol. 2008;190:892–901.