

# Angiography Offers Hope for Patients Suffering from Prostate-Related Urinary Disorders

By Chris Kraul

A minimally invasive catheterization technique known as prostatic artery embolization shows promise as an outpatient treatment for patients suffering from increasingly prevalent prostate hyperplasia. Pioneered by a Brazilian radiologist, the procedure began U.S. Food and Drug Administration approved trials this fall in twelve medical centers in the USA and Europe.



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Francisco Cesar Carnevale, MD, PhD, known as the pioneer of the prostatic artery embolization (PAE) procedure, has been Chief of Interventional Radiology at University of Sao Paulo Medical School since 2002.

A native of Sao Paulo, he studied medicine at the city's University of Mogi das Cruzes, and subsequently undertook fellowships and research stays at several U.S. institutions including the MD Anderson Cancer Center, the University of California-San Diego, and Beth Israel Deaconess Medical Center – Harvard Medical School, Boston, MA. He returned to the University of Sao Paulo in 1997 to complete a PhD in interventional radiology. He is a co-founder of the Brazilian Society of Interventional Radiology and Endovascular Surgery (SoBRICE). He has published over 50 peer-reviewed articles, as well as 25 book chapters on IR. The second edition of his vital reference book guide, *Radiologia Intervencionista e Cirurgia Endovascular*, originally published in 2006, is pending publication.

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# *“By lessening pressure on the urethra and easing the mechanical obstruction of the bladder, PAE enhances quality of life.”*

**Professor Francisco Cesar Carnevale, MD, PhD**

Department of Radiology, Interventional Radiology Section, University of Sao Paulo, Brazil

Uses of interventional catheterization have evolved far beyond the angioplasties that were its original focus. Increasingly versatile catheters, guided with the aid of angiography are competing with surgery to treat cases ranging from liver cancer and brain aneurysms, to uterine fibroids and faulty heart valves. This can save recovery time and costs for patients, while reducing the risk of post-operative complications and after-effects.

A procedure known as Prostatic Artery Embolization (PAE) has now joined angiography's therapeutic array as an option for men who suffer from benign prostatic hyperplasia (BPH), the principle cause of lower urinary tract symptoms experienced to some degree by around half the male population over 60. Symptoms include an increased frequency and urgency of urination, painful burning sensations, and intermittence of urinary stream due to mechanical compression of the urethra.

In simple terms, PAE involves the insertion of a catheter with a diameter of 2 mm at the femoral artery, which is then guided to the two main arteries feeding blood to the prostate gland. Safe catheter navigation is performed

under image guidance using Siemens angiographic equipment. When the catheter is in the correct position, microspheres are injected into the feeding arteries of the prostate in order to block blood flow. This creates an obstruction that can reduce the volume of the prostate by as much as 30–40 percent over the ensuing three months.

The shrinkage of the prostate in turn eases pressure on the urethra, allowing for better urine flow and a reduction in BPH symptoms.

Pioneered by Brazilian interventional radiologist Francisco Cesar Carnevale, a radiology professor at the University of Sao Paulo Medical School, the procedure is performed using Siemens imaging equipment and syngo DynaCT guidance and mapping software as an outpatient alternative for those who might otherwise have to resort to prostatectomies or a resection technique called TURP and laser, all of which require hospitalization.

### **Improved Quality of Life**

PAE is still a comparatively novel technique – approximately 1,000 patients have so far been treated

mainly in Brazil, Portugal, the USA and France. Other centers performing PAE are Italy, Spain, Russia and China. However, urologists and interventional radiologists are enthused by early results that show prostate shrinkage and positive outcomes for quality of life.

“By lessening pressure on the urethra and easing the mechanical obstruction of the bladder, PAE enhances quality of life. And if you have extreme BPH symptoms, life can be miserable. In extreme cases, patients may require permanent catheterization or have to self-catheterize every time they have to urinate,” Carnevale explains. “A common symptom among BPH sufferers is nocturia – waking up several times a night to urinate, which causes loss of sleep and makes you tired at work the next day.”

The bonus for PAE recipients is that they go home the same day and suffer none of the possible TURP-associated side effects such as retrograde ejaculation and temporary incontinence.

The new treatment is entering a critical stage this fall with the launching

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of the first large-scale clinical trial under the auspices of the U.S. Food and Drug Administration (FDA). Carnevale will act as principal investigator in the trial. The four-year test will track 186 patients in twelve USA and European hospitals to compare the experience of patients that undergo PAE with those treated with TURP.

#### **The Cost of BPH**

Success in FDA trials could significantly impact BPH protocols. Data from a study in 2005 show that treatment of the condition costs an estimated 3.9 billion U.S. dollars annually and accounts for up to 38 million lost hours of worker productivity. Authors said BPH patients also make 4.4 million medical office appointments and more than 117,000 emergency room visits. More than 105,000 patients are hospitalized in the U.S. each year.

Incidences of highly prevalent BPH is likely to rise in the foreseeable future as the global male population lives longer. Environmental factors including rising obesity, diabetes, and sedentary lifestyles are also fueling increased reporting of enlarged prostates – which is not

necessarily an indicator or precursor of prostate cancer.

#### **Advantages of PAE**

While TURP has been recognized with excellent efficacy in prostate size reduction and symptoms relief, it can also carry the risk of retrograde ejaculation, which means sperm and seminal liquid are ejaculated into the bladder, instead of out through the penis. TURP also requires general, intradural or peridural anesthesia, whereas PAE patients receive only local anesthesia.

#### **Disadvantages of PAE?**

Carnevale explains that the use of angiography means doctors, patients, and medical technicians are exposed to radiation for 30–40 minutes during the two-hour procedure, although Siemens engineers are working to reduce fluoroscopy time and dose based on proprietary Artis low-dose software. Another risk is that some patients' kidneys react poorly to contrast agents used in angiography, which can cause renal failure in rare instances.

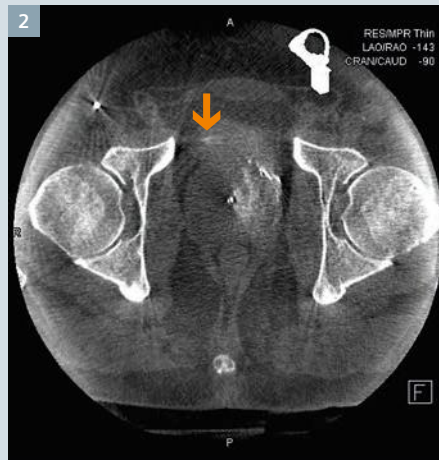
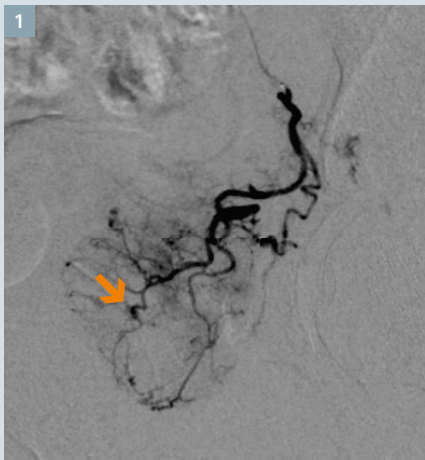
It is crucial to occlude both left and right prostatic artery since unilateral embolization can lead to recurrence.

In Sao Paulo, 92% of the patients are embolized bilaterally. “This is how we define technical success of a PAE procedure.” However bilateral embolization goes along with longer procedure and fluoroscopy times and a higher amount of contrast medium used. “Therefore we need to make use of all available measures to reduce dose for patient and staff. We all use protective goggles and clothing and Siemens CARE+CLEAR to lower the dose. In some interventions we even have performed the procedure with as little as 20–30 minutes fluoroscopy time,” Carnevale said.

#### **Avoiding Non-Targeted Embolization with syngo DynaCT**

Low-dose imaging is one of the many advantages that derive from working with Siemens, according to Carnevale. Others include after-sales consultation and engineering, image clarity, and user friendly syngo DynaCT software.

“syngo DynaCT is the most important software for the embolization procedure because it identifies the arteries feeding the prostate. It can guide you to where you have to go with the microcatheter. While I'm working, it also gives me an idea of the percent-



- 1 Digital subtraction arteriogram (DSA) with the microcatheter positioned into the left inferior vesical artery (left ipsilateral oblique perspective) previously to the left lobe prostate embolization. Note the opacification of the left intraprostatic branches. Procedure performed using the Artis zeego.
- 2 syngo DynaCT with reduced dose acquired before embolization of left prostatic lobe shows risk of non-target embolization of bladder wall (arrow). In addition, only partial left prostate enhancement is observed indicating either additional prostatic feeder or catheter position being too distal.

age of the prostate I am treating,” Carnevale said. “Even more importantly, it helps me avoid non-targeted embolization – the areas I don’t want to affect – because with syngo DynaCT, we can identify the arteries feeding the non-targeted organs.”

The idea for PAE came to Carnevale in 2006 after he had read an article in a medical journal about doctors who used embolization to stop a patient’s persistent BPH-related prostate bleeding. In a one-year follow-up of this case, the doctors noticed that in addition to a stop to the bleeding, the embolization caused a reduction in prostate size and an improvement in his quality of life by easing urinary tract symptoms.

“It was just an observation, but we thought, why not look at prostate embolization as a therapy for BPH,” Carnevale said. Fortunately, he was invited and moved to Harvard University in 2007 on a research grant and was able to test the theory by embolizing animals with that group. They injected resin microspheres into the prostate arteries of six dogs and one month later, saw that the dogs’ prostate glands had shrunk by 40 percent. He then knew he was on to something.

#### FDA study launched

Since Carnevale administered the first PAE procedure in 2008 at the University of Sao Paulo Medical School, the use of the technique has slowly grown. In recent years, he helped set up training centers in Paris, Zaragoza and Milan. He has trained close to 30 interventional radiologists in the procedure. Recently, he went to Mount Sinai and Johns Hopkins, both in the USA, where he launched the FDA trial by treating the first of 186 patients in the test population.

“The fact that we have developed this technique and are pioneers in training doctors on several continents in its use is adding to Brazil’s medical prestige,” Carnevale said, who is aware of the economic condition in health care in his country. And he finalizes “this is very important for our department, our university and our country.”

A former foreign correspondent for the Los Angeles Times, **Chris Kraul** is a Bogota-based freelance writer who specializes in economics, healthcare, and the environment.

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# The Benefits of PAE over TURP: “Fewer Minor and Major Complications”

Marc Sapoval, MD, PhD, Head of the Vascular and Oncological Interventional Radiology Department at the Hôpital Européen Georges Pompidou in Paris, France, and Olivier Pellerin, MD, Deputy Head of Interventional Radiology talk about the practical aspects of prostate artery embolization (PAE) to treat benign prostatic hyperplasia (BPH).



Marc Sapoval, MD, PhD, is Professor of Clinical Radiology and Chair of the Vascular and Oncological Interventional Radiology Department at Hôpital Européen Georges Pompidou in Paris, France. He is co-founder and course director of the Global Embolization Symposium and Technologies (GEST). He also served as 2008 – 2009 Program Chairman for the Cardiovascular and Interventional Radiological Society of Europe. Holder of a PhD as well as an MD, Marc Sapoval is an expert in the area of renal disease.



Olivier Pellerin, MD, is Assistant Professor of Clinical Radiology at Hôpital Européen Georges Pompidou in Paris. He was a visiting research radiologist at Johns Hopkins University in 2011 – 2012 and has authored or co-authored more than 30 peer-reviewed publications. Since 2013, Marc Sapoval and Olivier Pellerin have trained more than 30 radiologists from several countries in the PAE technique.

What are the complexities and risks of PAE?

**Sapoval:** PAE is a complex procedure. The target arteries are small and difficult to access and there are a lot of anastomoses and tiny vessels that go to the bladder, rectum and penis that you don't want to embolize. In PAE you need to be 100% sure to block the appropriate artery.

Please describe the optimal patient for PAE.

**Sapoval:** PAE is particularly suitable for relatively young patients – say less than 70 – as they are easier to catheterize. Patients with large prostates around 80 g benefit the most from the treatment. It's also an eligible treatment option for patients who are afraid of or don't qualify for surgical therapy. We would not treat patients at risk or with suspected cancer.

What is the workflow for PAE treatment?

**Sapoval:** Patients are referred to us by urologists and sometimes directly through various communication pathways. In this case we send the patient to the urologist in order to allow multidisciplinary assessment. In the pre-procedure phase we as a board of specialists all come together to collate all the pertinent information including scores like PSA (prostate-specific antigen), urinary flow max, IPSS (International Prostate Symptom Score) and QoL (Quality of Life) as well as imaging information such as MR, MRA, and echographs of the prostate. We discuss treatment with the patient and staff and make sure the case is suitable for PAE. We explain that we have a success rate of between 80 and 90 percent and that we've never had major complications.

When preparing the patient for the intervention, we place a foley catheter in the bladder that we use as additional landmark during the procedure. For assessing the vascular anatomy of the pelvic region, we acquire a *syngo* DynaCT at the very start of the procedure. We study this dataset thoroughly to understand the vascular supply of the prostate and neighboring organs such as bladder, rectum and penis. And we use it for access path planning using *syngo* Embolization Guidance. The planning data is overlaid on live fluoroscopy to guide us in catheter navigation.

After having positioned the micro-catheter according to the planning, we perform another DynaCT. It visualizes which portion of the prostate will be affected by embolization from this catheter position, but it also reveals potential areas of non-target embolization. When we see the catheter position is safe and ensures embolization of left or right prostate portion, we slowly inject microspheres until stasis is reached.

#### **How much training is required to perform the procedure and why is it essential?**

**Sapoval:** You need to have an in depth understanding of the anatomy and the potential complications. You also need to learn imaging skills to get the necessary confidence to begin performing PAE. First, interested doctors go to conferences and expert meetings. Then, they can come to our institution for two days in groups of five or six. They are exposed to lectures and previous case studies, and they observe at least three live cases to see how the procedure is performed with all the difficulties and problems. Later, we go to their medical centers to follow up. So far we have taught the procedure to about 30 people since 2013.

#### **How important is Siemens technology to the success of PAE?**

**Sapoval:** PAE is still a new technique and Siemens knows PAE is challenging technically. Therefore Siemens has developed several imaging tools that help us do the procedure with more confidence, and we are working with Siemens engineers to refine the tech-

nological support and make it easier and safer.

Most important software applications today are *syngo* DynaCT, providing intraprocedural CT-like crosssectional imaging, and *syngo* Embolization Guidance for access path planning.

#### **Can you discuss the various Siemens PAE software applications and how they help?**

**Pellerin:** *syngo* DynaCT serves two main purposes during the procedure. First, it allows us to assess the vascular anatomy and define target vessel(s) in the beginning of the intervention. Second – and even more important esp. in PAE – it is a crucial intraprocedural tool to confirm safe catheter position for embolization, avoiding non-target embolization.

In the context of the very complex pelvic vessel anatomy, access path planning and guidance during catheter navigation is a very much desired support functionality. This is where *syngo* Embolization Guidance comes into play as a navigation tool to the prostate. It helps speed up the procedure and thereby facilitates reduction of fluoroscopy time and contrast material.

And there is the exciting possibility of assessing the functionality of tissue using *syngo* DynaPBV Body. This software can help you quantify the reduction in blood volume in the prostate due to PAE by making comparisons of the blood volume maps from before and after the procedure. We hope in the future it will prove to be predictive and well correlated with results, but we still need further mid-term clinical studies to provide evidence.

#### **Is dose reduction an important factor in PAE?**

**Sapoval:** It's the way we have to work as we stand every day in the Angio lab and for the patient, this is a very dose sensitive area of the body.

**Pellerin:** The PAE procedure is still quite long, at least one and a half hours, but we apply radiation only while we are manipulating the

catheter and embolizing the target. That adds up to about 40 minutes of radiation. However, we are just in the initial phase, and intervention time and radiation dose will decrease with experience. Moreover, through our collaboration with Siemens, we will find technical ways to reduce dose in addition to the already existing wide range of CARE options that come with each Artis system.

If patient size allows, we apply low-dose fluoroscopy at very low framerates. And we constantly use the DynaCT Body Care protocol – a dedicated cone-beam CT that saves more than 30% of dose compared to standard DynaCT.

If anatomy allows, we even collimate our DynaCTs cranial/caudally to expose the patient and ourselves to as little dose as possible. Due to the fact that we are working in a region with extremely small and fragile vessels most DynaCTs are done with manual injection which requires us to stand table-side during the rotational angiography. And as mentioned before, the use of navigation tools reduces fluoroscopy time and therefore overall dose.

#### **Based on the experiences you gained so far – Are all signs for PAE being an effective treatment of BPH positive?**

**Sapoval:** It's too soon to measure the complications in a really large number of medical centers. And we don't have the answers to long-term questions such as relapse rate because the procedure is too new. But the basic message so far is that with PAE you have the same results as with TURP but with fewer minor and major complications, especially sexual dysfunction. That's why it's important for us that Siemens is really focused on understanding what we need to improve our results and our safety in specific clinical situations.

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# Benign Prostatic Hyperplasia Supported by *syngo* DynaCT

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## Patient History

A 66-year-old male with benign prostatic hyperplasia (BPH). Received drug treatment (alpha blockers and 5 alpha reductase inhibitors) for one year. Symptoms worsened gradually to the point where the patient needed invasive treatment due to a major dysuria. Patient rejected transurethral resection of the prostate (TURP) because he was afraid of potential side effects such as urinary incontinence or impact on sexual life. Patient was referred to interventional radiology for prostatic artery embolization after multidisciplinary discussion.

## Diagnosis

Prostate volume: 60g, Prostate-specific Antigen (PSA): 0.85, International Prostate Symptom Score (IPSS): 13; Quality of Life (QoL): 4; Flow Max 5ml/s

Professor Marc Sapoval, MD, PhD



## Treatment

Bilateral prostatic artery embolization using 300–500 µm Embospheres® (Merit Medical). Homogeneous solution of 2 cc spheres combined with 10 cc contrast agent and 10 cc saline. Fathom™ .014" steerable microwire (Boston Scientific) and 2 Fr Progreat® Microcatheter (Terumo).

Assessment of prostate in pre-interventional MRI for identification of central gland and transitional/peripheral zone before intervention.

Foley catheter filled with contrast medium and saline placed and used as basic landmark in 2D imaging.

*syngo* DynaCT imaging when catheter in left/right iliac artery for assessment of 3D vessel tree and identification of prostatic arteries using access path planning software *syngo* Embolization Guidance (Fig. 1A, 1B).

*syngo* DynaCT with reduced dose (5s *syngo* DynaCT Body CARE protocol, 248 projections) with hand injection of diluted contrast agent via catheter in right prostatic artery to exclude non-target embolization (Fig. 3A, 3B). This CBCT was acquired with the angiography system on the left side of the table to reach pelvic area also in taller patients.

Successful superselective embolization with very slow injection into right and left prostatic artery until stasis was reached.

## Comments

The procedure requires a thorough understanding of the vascular anatomy and use of CBCT technology to exclude non-target embolization. It was possible to show that a 5s *syngo* DynaCT Body CARE run provides sufficient image quality to confirm safe catheter position, while saving about 37% dose compared with a regular 6s *syngo* DynaCT Body.

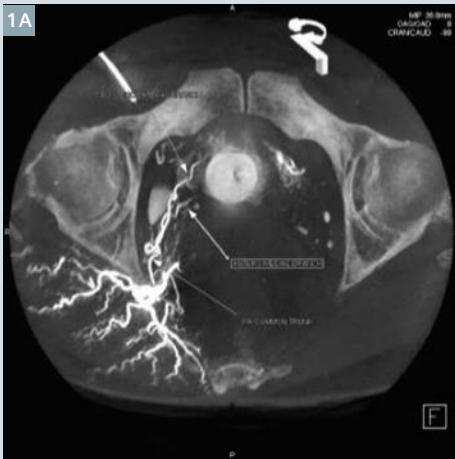
Injection of diluted contrast is mandatory to obtain optimal *syngo* DynaCT imaging.

With cranial/caudal collimation during *syngo* DynaCT acquisitions, dose can be reduced while image quality improves even further due to less scatter radiation.

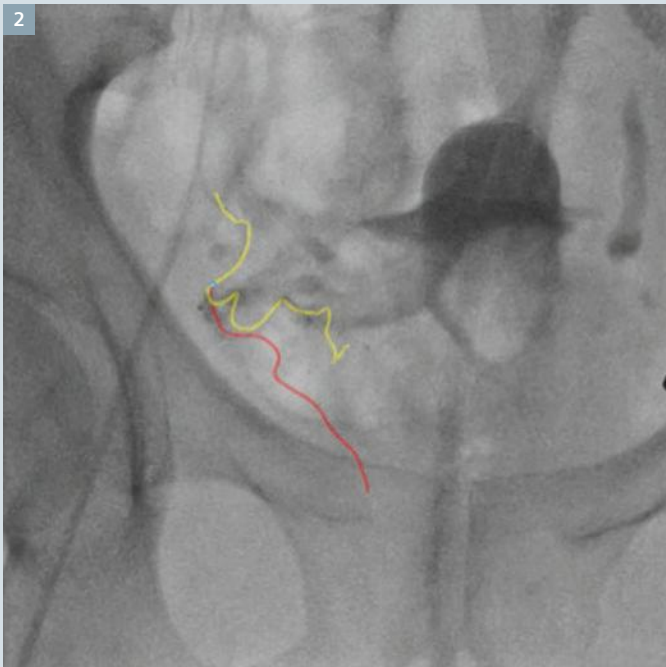
*syngo* Embolization Guidance for faster navigation to the target vessel saves contrast media, shortens fluoroscopy time, and enables dose reduction (Fig. 2).

## Contact

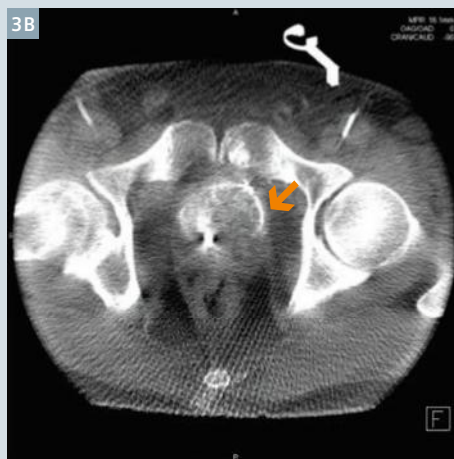
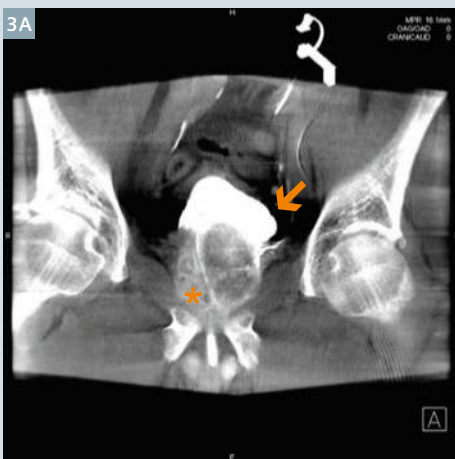
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1 Axial and coronal views can help to identify the prostate artery feeders. Here, an antero-medial and postero-medial branch are visible.



2 Store fluoro showing overlay of syngo Embolization Guidance centerlines (yellow line represents the anterosuperior branch to the right prostatic artery).



3 A syngo DynaCT (5s syngo DynaCT Body CARE protocol, 248 projections) is performed before starting the embolization. It confirms the safe catheter position into the prostate artery away from non-target arteries (rectal/vesical branches). Coronal and axial view with arterial contrast media injection show a right lobe contrast staining (\*), without vesical or rectal wall enhancement. Arrows point to contrast agent in the bladder.