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Contrast modulation in chronic total occlusion percutaneous coronary intervention

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Abstract

The intraplaque injection of contrast media in the recanalization of coronary chronic total occlusions (CTO) has witnessed a dynamic journey since its initial formulation. Contrast-guided subintimal tracking and re-entry (STAR) was the first contrast modulation technique for CTO percutaneous coronary intervention (PCI). With this technique, a forceful injection of a large volume of contrast (3–4 mL) was performed in order to achieve hydraulic recanalization of the vessel. This approach was associated with extensive vessel injury and unpredictable true lumen re-entry, which were in turn linked to high rates of restenosis on follow-up. In the subsequent iteration, called the “microchannel technique”, a smaller amount of contrast media (1 mL) was gently injected inside the plaque to modify its compliance by softening and recruiting loose tissue, which facilitated subsequent true-to-true lumen crossing with a polymer-jacketed wire along paths of least resistance. The microchannel technique has later evolved into what is currently known as the “Carlino technique”, where a minimal volume of contrast media (<0.5 mL) is gently injected inside the occlusion, with the goal of modifying plaque compliance to facilitate guidewire and microcatheter advancement through a fibrocalcific plaque. The Carlino technique is now widely utilized to allow negotiation of difficult-to-cross occlusions, particularly by the “hybrid operators”, with high success rates and low incidence of complications. The purpose of this article is to provide a historical perspective on the use of contrast modulation in CTO PCI, its pathophysiological basis, as well as technical recommendations on how and when to perform these maneuvers.

KEYWORDS

Carlino, chronic total occlusion, contrast, microinjection, percutaneous coronary intervention

Contrast media injection, frequently referred to as the “Carlino technique”, is a useful technique in the recanalization of coronary chronic total occlusions (CTO). However, description of its use has been presented at different forums (congresses, social media, etc.) in a way that differs markedly from its original description. Specifically, confusion exists since many incorrectly utilize this term to refer to any form of contrast media injection within the occlusion. The majority of operators using this maneuver regard it as a way to obtain a microdissection. As we will describe in this manuscript, however, the primary goal of this technique is to modify plaque compliance, by means of an intra-plaque contrast injection, striving not to extend the contrast into the subintimal space. The purpose of this article is to provide a historical perspective on the use of contrast modulation in CTO percutaneous coronary intervention (PCI), its pathophysiological basis, as well as technical recommendations on how and when to perform these maneuvers.

A decade ago, success rates for CTO PCI were low, averaging 60–80%. Antegrade wire escalation was the primary, and frequently only, technique used by most operators.

The lack of now widely available high-performance CTO devices, such as microcatheters (over-the-wire [OTW] balloons were used instead) and CTO guidewires (only nondedicated wires were available), may have contributed to previously suboptimal success rates.[1]

In this context, the introduction of subintimal techniques, namely subintimal tracking and re-entry (STAR),[2] represented a major breakthrough, since it allowed recanalization of complex occlusions that

FIGURE 1 Two examples of tubular dissection

had low likelihood of success using a conventional wire escalation approach.

Furthermore, it introduced the feasibility of using the subintimal space for CTO crossing, which was previously considered a forbidden territory that, when entered, often signaled the end of the procedure. The STAR technique had, however, some major limitations, such as high rates of restenosis, need for significant operator expertise and, if performed improperly, non-negligible risk of perforation.[3]

To overcome the limitations of STAR, our group developed the "contrast-guided STAR" technique, which represented a paradigm shift in the field, being the first example of safe and effective use of contrast modulation in CTO PCI. Briefly, a forceful injection of a moderate volume (3–4 mL) of contrast media were performed through the OTW balloon within the occlusion. The goal of this maneuver was twofold: (1) delineate gear localization within the occlusion; (2) possibly achieving direct dye penetration into the occlusion and

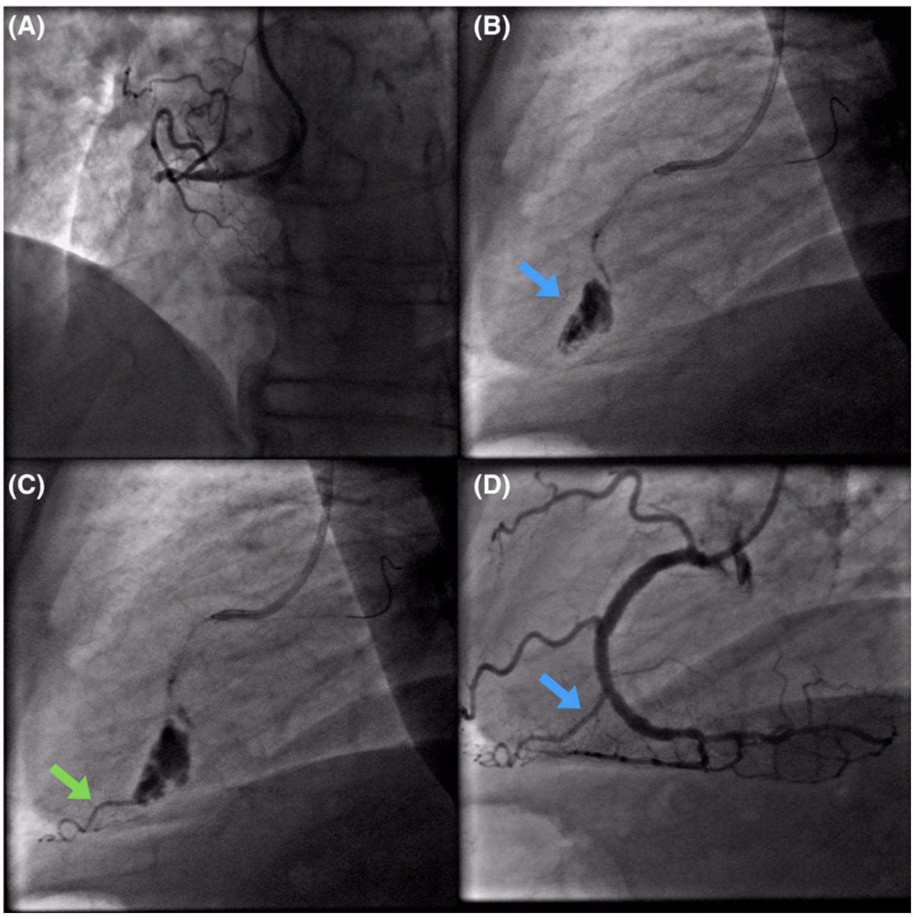

FIGURE 2 Storm-cloud dissection. A, Proximal right coronary artery chronic total occlusion. B, Contrast injection through the over-the-wire balloon in a small side branch causes transient alteration of periadventitial permeability, which resembles a perforation (arrow). C, However, further contrast injection causes distal recanalization of this small branch (arrow). D, Final angiogram showing recanalization of the occlusion and complete healing of the storm-cloud dissection (arrow) [Color figure can be viewed at wileyonlinelibrary.com]

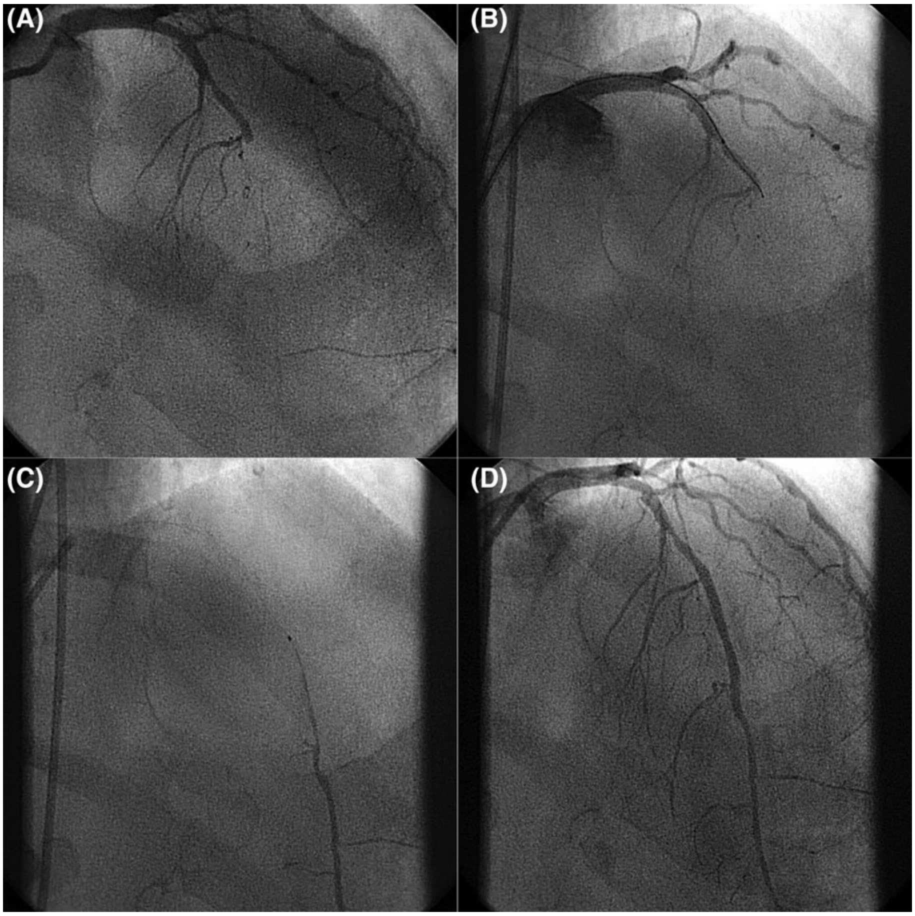

FIGURE 3 Microchannel technique. A, Mid left anterior descending chronic total occlusion. B, The proximal cap is punctured through the microcatheter in a central location. C, The microcatheter is advanced half-way through the occlusion and a small amount of contrast media is gently injected, achieving distal vessel visualization. A polymer-jacketed guidewire is then easily advanced through the occlusion and the procedure is completed as per standard practice, (D) with a good final result

recanalizing the vessel. With regards to the first aspect, two kinds of result could be obtained with contrast-guided STAR. The first is called "tubular dissection", which has a linear morphology consistent with the vessel outline, probably because the contrast lies between the media and the adventitia of a large vessel, whose subintimal space can accommodate the considerable amount of injected contrast (Figure 1). Tubular dissection often led to vessel recanalization by fenestration of the subintimal space into the true lumen. The second type of angiographic result (Figure 2) is called "storm-cloud dissection" which is a diffuse and inhomogeneous staining of contrast media that was often confused with a perforation. Storm-cloud dissection likely indicated contrast extravasation in the periadventitial space and corresponded to a transient alteration in vessel permeability,[4] which—in our experience—usually self-resolved within a few minutes. This angiographic image is seen following contrast injection into a small vessel, whose subintimal space cannot accommodate the injected volume, or when the subintimal space is heavily calcified or fibrotic, thus limiting the progression of the injected contrast.

Contrast-guided STAR paved the way to a safer approach to the recanalization of complex occlusions. In the original publication,[5] angiographic success was achieved in 81%, with a 71% rate of complete recanalization. Perforations were observed in 4% of cases (which was lower than the 10% observed with the original STAR).[2] At a median follow-up of 209 days, the incidence of target-lesion revascularization using first-generation drug-eluting stents was 29%. Contrast-guided STAR was later abandoned, mainly due to the unpredictability of the site of true lumen re-entry, which often led to long total stent lengths (which in turn were associated with high rates of restenosis), and loss of side branches.[3] These factors in turn often contributed to compromising vessel runoff, which has also been associated with risk of restenosis on follow-up.[6]

Contrast injection was subsequently modified as follows: (1) injected contrast volume was reduced to the smallest amount of dye able to provide adequate visualization; (2) the injection force was tailored to the perception of resistance and visual feedback; (3) contrast media was injected in an intra-plaque location. All these modifications led to the development of the so called "microchannel technique",[7] where 1 mL of contrast was gently injected through the microcatheter immediately after penetrating the proximal cap of the occlusion centrally and advancing for just a few millimeters (Figure 3). Performing this maneuver was often associated with direct visualization of the distal true lumen (by means of contrast-induced intraplaque microchannel recruitment), and subsequent occlusion crossing utilizing low-tipload guidewires. The rationale behind this technique was the contrast-induced hydraulic dilatation of the microchannels, which were then engaged by the guidewire. These anatomic

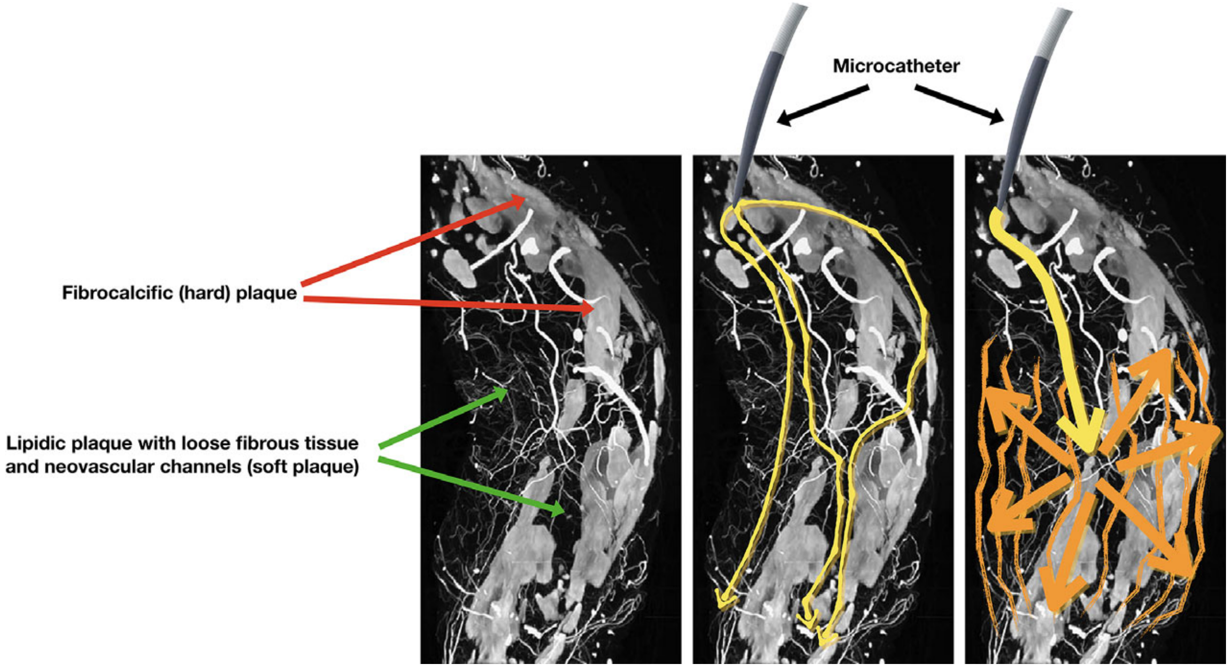

FIGURE 4 CTO histopathology and its interaction with contrast media injection. If a small volume of contrast is gently injected (thin yellow arrows), it will travel through the paths of least resistance through the occlusion. On the other hand, if a forceful injection of a larger contrast volume is performed (thick yellow arrow), it will cause contrast redistribution toward the subintimal space (thick orange arrows) with subsequent periadventitial staining (orange lines) [Color figure can be viewed at wileyonlinelibrary.com]

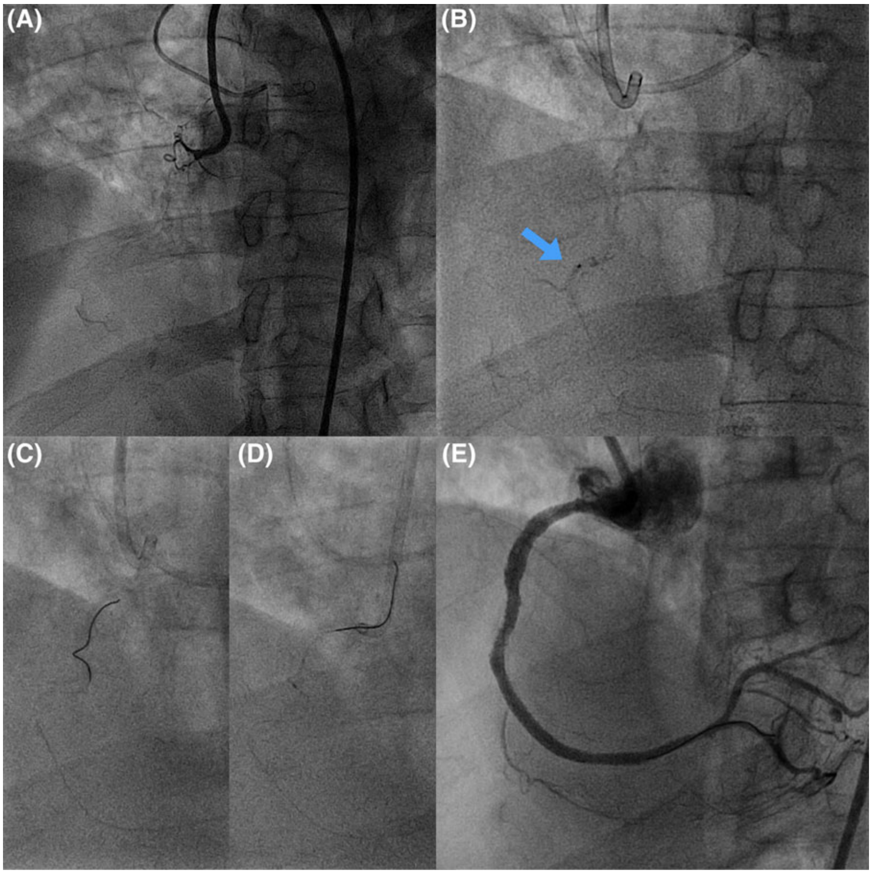

FIGURE 5 Carlino technique—uncrossable lesion. A, Ostial, severely calcified and tortuous right coronary artery chronic total occlusion. B, Retrograde Carlino technique (arrow). C, D, true-to-true crossing is then easily achieved with a polymer-jacketed guidewire despite vessel tortuosity and calcification. E, Final result, with moderate stent underexpansion in the mid segment, despite very high pressure postdilatation with specialty balloon, due to very severe vessel calcification [Color figure can be viewed at wileyonlinelibrary.com]

structures have a diameter of 100–200 μm (sometimes up to 500 μm).[4] In an experimental model of CTO (thrombin injection in rabbit femoral arteries),[8] microcomputed tomography imaging demonstrated the development of corkscrew-like microchannels starting at the proximal cap at 6 weeks. However, this recanalization pattern regressed at later time points (12–24 weeks). This observation, coupled with the fact that most CTO guidewires have larger tip diameter (0.014″ = 360 μm) than most microchannels, suggested that the actual mechanistic principle behind occlusion recanalization with contrast microinjection was different. This could involve alteration of plaque compliance by softening and recruiting the loose tissue through injection of a viscous fluid, which facilitated subsequent crossing with a polymer-jacketed wire along paths of least resistance.

The microchannel technique has evolved into what is currently known as the "Carlino technique".[9] In the current iteration, an even smaller volume of contrast media (<0.5 mL) is injected inside the occlusion, with the goal of modifying plaque compliance to facilitate guidewire and microcatheter advancement through a fibrocalcific plaque. Knowledge and understanding of CTO histopathology may explain why this maneuver can be effective. Figure 4 shows a three-dimensional long axis view of a microcomputed tomography of a CTO with a patchy fibro-calcific content (large fibro-calcific regions without neovascular channels), intermingled with loose tissue segments representing the soft plaque of the CTO, which is more likely to allow wire passage into the distal lumen. The rationale behind the gentle injection of a small amount of contrast within the occlusion is based upon the generation of hydraulic forces along the longitudinal axis of the involved vessel. The contrast will follow the path of least resistance, represented by the loose tissue segments within the occlusion, thus decreasing the friction upon subsequent guidewire advancement. If, however, the amount of contrast or the injection pressure is increased, the intraocclusion presence of areas of high-resistance (fibro-calcific plaques) will divert hydraulic forces in a radial direction, thus involving the subintimal space, which is usually softer than the intraluminal obstructing material. This will in turn lead to contrast extravasation in the periadventitial space, and the operator will promptly stop contrast injection to minimize the extent of subintimal hematoma. Figure 5 shows an example of this technique. The Carlino technique is now widely utilized (particularly by the so called "hybrid operators") to allow negotiation of difficult-to-cross occlusions, when support-enhancing techniques and balloon dilatation have failed, with high success rates and low incidence of complications.[10] Another useful application of the Carlino technique is to provide information about microcatheter localization within the

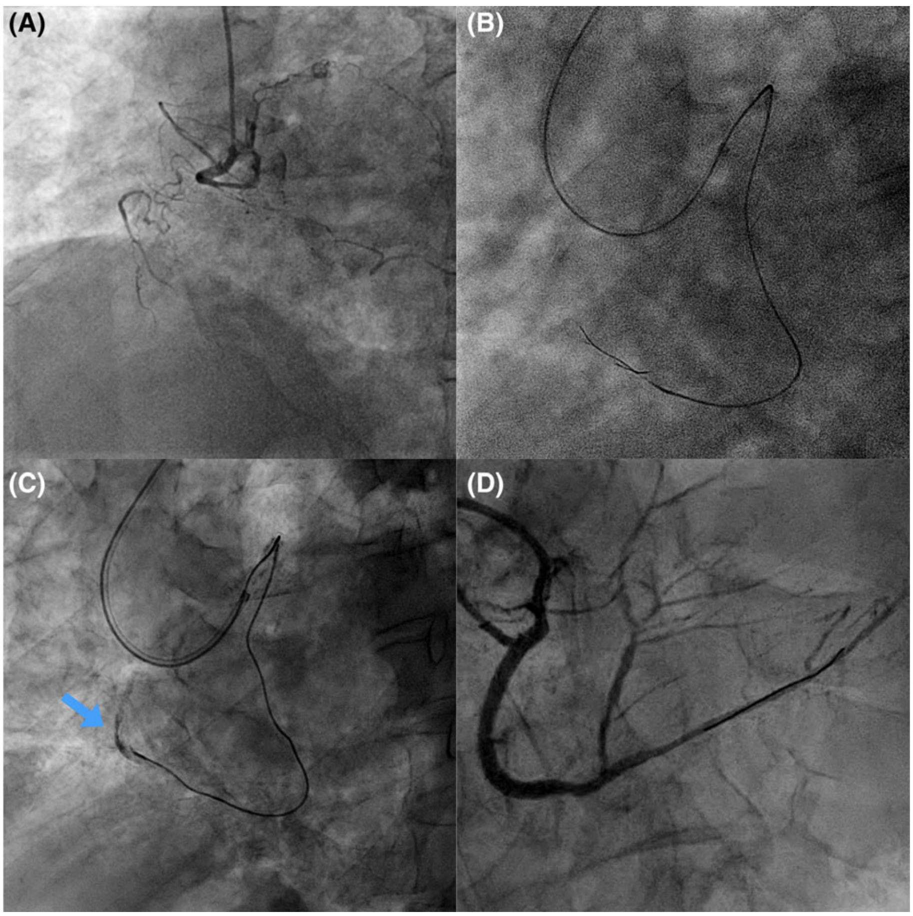

FIGURE 6 Carlino technique—understanding gear position within vessel architecture. A, Proximal right coronary artery (RCA) chronic total occlusion. B, After retrograde crossing through a first septal channel toward the posterolateral branch, a knuckle wire was advanced into what was thought to be the distal RCA. However, the operator was unsure about vessel track, and C, decided to inject a small volume of contrast before further advancing the knuckle wire (arrow). This in fact revealed correct position within a large vessel (tubular dissection) corresponding to the mid RCA, and the occlusion was then recanalized with reverse controlled antegrade and retrograde subintimal tracking, with D, optimal final result [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Applications of the Carlino technique in the context of the "expanded hybrid algorithm"

Procedural scenario	Aim of the Carlino technique
Impenetrable cap	Hydraulic microdissection of the cap to facilitate subsequent wiring attempts
Wire across cap/lesion but gear will not follow	Modify plaque compliance to facilitate subsequent device advancement
Unclear gear location within the vessel	Clarify microcatheter position within the vessel architecture
Wire/gear track into a side branch at the proximal/ distal cap or within the occlusion	Define microcatheter position at the bifurcation and cause dissection into the main vessel to better inform a re-attempt at a wire re-direct
Difficulty crossing due to graft insertion (suture line)	Define anatomy and try to dissect suture line

vessel architecture (intraplaque vs. subintimal in main vessel ["tubular dissection"] vs. subintimal in a small vessel ["storm-cloud dissection"]), similar to what has already been described for contrast-guided STAR. However, in this refinement of the technique, a much smaller volume of contrast is gently injected in order to limit vessel disruption as much as possible (Figure 6). A complete description of the applications of the Carlino technique in the context of the "expanded hybrid algorithm" is provided in Table 1.

As outlined above, contrast modulation in CTO PCI has witnessed a long and dynamic journey, still being an evolving concept. Summarizing, after initial formulation in the now abandoned contrast-guided STAR, the microchannel technique paved the way to further refinement and clarification of its mechanics into the currently used Carlino technique, which is ultimately the only contrast modulation strategy recommended by these authors. We believe that a correct understanding of the principles outlined in this article is fundamental to promote a safer, more effective, and broader application of contrast modulation in CTO PCI.

CONFLICT OF INTEREST

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