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Computed tomography as a tool for percutaneous coronary intervention of chronic total occlusions

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Abstract

Chronic total occlusions (CTO) constitute a major challenge in percutaneous coronary revascularisation (PCI). The development of new interventional strategies, the availability of purpose made tools including dedicated catheters and wires, as well as increasing expertise by the operators, have contributed to the modest success rates which today hover around 75%. Case selection is of utmost importance since failure of this high risk procedure with its typically high radiation doses, high contrast doses and increased complication rates is associated with long term adverse events. Imaging of the coronary arteries using the gold standard of invasive coronary angiography allows characterisation of the chronic total occlusion and is often able to predict the probability of successful recanalisation. Multislice computed tomography (MSCT) is increasingly being utilised as a non-invasive diagnostic imaging modality to detect coronary artery disease. Its ability to provide information on the soft tissue (including plaque) surrounding the lumen has been applied to better define the morphological features of CTOs. In fact, the amount of calcification, tortuousity and actual length of the occluded segment which are established predictors of success, are all better characterised by MSCT. Three dimensional reconstruction of the coronary anatomy and its integration with two dimensional fluoroscopy images during the actual CTO-PCI procedure may help to identify the best angiographic projection, offering a directional guide at the angiographically "missing segment". More technological advances are needed to optimise this multi-modality imaging integration. Whether this will result in better success rates for CTO-PCI is still the subject of ongoing research. It is then that we can evaluate the true benefit of the use of MSCT for CTO against the risk from excessive radiation associated with this strategy.

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Introduction

Chronic total occlusions (CTO) can be found in a third of patients referred for diagnostic invasive coronary angiography.[1] CTOs are angiographically defined as an obstruction of a native coronary artery with no luminal continuity and interruption of antegrade flow with thrombolysis in myocardial infarction (TIMI) grade 0 or 1 and occlusion period exceeding three months. The incidence of such lesions in patients considered for revascularisation is considerable at around 50%.[2] Restoration of flow in the CTO is associated with improvement in anginal symptoms[3], left ventricular function[4] and long-term survival[5] especially in patients with reversible ischaemia in the relevant myocardial territory.[6] The choice of treatment strategy, namely PCI, coronary artery bypass graft surgery (CABG) or conservative medical management depends on the symptoms, documented ischaemia, presence of multivessel disease and the general condition of the patient. Despite the comparability of outcomes between PCI and CABG, especially in the era of drug-eluting stents, CTO is still one of the main reasons for referral to CABG.[7] This is due to the high-risk nature of PCI in CTO which is associated with prolonged procedure time, increased radiation dose, increased contrast use, high complication rate and low success rate when compared to PCI in non-CTO vessels.[8-10]

Once successful PCI is achieved, however, the prognosis is comparable to PCI in non-CTO vessels, while major adverse cardiac events (MACE) in those patients with unsuccessful attempts are more frequent (30 day MACE: 5.5% vs. 14.8%).[11] Therefore, careful selection of those patients that are most likely to benefit by having a good chance of a successful PCI remains essential. Until recently, much of this depended on the morphological appearance of the coronary anatomy on invasive coronary angiography.[8,12]

Multislice computed tomography (MSCT) has now been established as the best non-invasive diagnostic imaging modality of the coronary arteries, and it is gaining increasing and more widespread use.[13] Its ability to convey information that goes beyond the lumenogram has attracted considerable interest. It is clear that differential imaging of soft tissue in the coronary wall (including plaques) and its surroundings make it an attractive tool for characterisation of CTOs.[14,15] Moreover, the development of new hardware and software tools that allow three dimensional reconstruction and integration with intra-procedural fluoroscopic views may provide a new dimension in the treatment of CTOs.[16]

The aim of this review is to explore the established and potential benefits that computed tomographic angiography brings to the treatment of CTOs, while recognising its hazards and limitations.

CTO pathophysiology and histological appearance

Chronic total occlusions are most common in the right coronary artery (RCA) and least common in the left circumflex artery (LCx). They develop at sites of fibro-atheromatous plaques after an acute thrombotic occlusion. Persistence of occlusion results in thrombus organisation and with increasing age, the components of the CTO, including old lumen, intimal plaque and adventitia, undergo varying degrees of compositional changes. The old lumen is mainly composed of organised thrombus with extensive recanalisation. A tough fibrous cap is often present at the proximal and distal margins. The intimal plaque is mainly cholesterol laden or mixed with low levels of collagen, calcium and elastin in CTOs of less than a year of age. Fibrocalcific intimal plaque with more than 25% calcium, elastin and collagen tend to be more common in older CTOs. The calcium is observed to increase with advancing CTO age. Neovascularisation channels occur extensively both in the intimal plaque and in the adventitia. Here they often communicate with the adventitial vasa vasorum[17].

Interestingly, less than half of CTOs show a 100% occlusion at autopsy. There also seems to be no relation between the severity of the stenosis caused by the plaque and the plaque composition or the lesion age.[17]

There is, therefore, a relationship between the amount of calcium in a CTO, its collagen content and its age. Availability of a patent residual lumen (or recanalisation channel) and age-related changes in intimal plaque composition and their identification with imaging techniques may be key determinants of successful guide wire passage and dilation of the CTO.

Appearance of CTO on MSCT

Chronic total occlusions appear as a complete lack of contrast opacification of the artery lumen on MSCT axial images, multiplanar reformations (MPR) and maximum-intensity projections (MIP). The distal vessel lumen is often opacified, although less intensely, via filling of collaterals. In fact lack of contrast in the distal segment should raise the suspicion of an acute or subacute occlusion which is usually associated with higher success rates of PCI. The occluded segment usually has a different attenuation from the surrounding non-vascular tissue and can be readily identified. Nonetheless, post-processing reconstructions (MPR, MIP and three dimensional volume rendering) require substantial manual input and erroneous tracking of arteries to large side branches can lead to missed diagnosis. Also differentiation between total and subtotal occlusions is not reliable with MSCT, in part due to its limited spatial resolution. Longitudinal sections and cross-sectional images of the occluded segment may reveal varying degrees and patterns of calcification. Three dimensional volume rendering (3D VR) images allow proper visualisation of the orientation of the different segments of coronary arteries in space since they can be rotated around any axis. This provides better understanding of the characteristics of the vessel as well as the "missing segment" especially length, tortuosity, angles with side branches, blunt or tapered stump, calibre of distal vessel, etc. (see Figure 1)

MSCT is more sensitive in detecting, quantifying and localising calcification in non-occluded vessels when compared to invasive angiography.[10,18] Using intravascular ultrasound (IVUS) and IVUS-derived virtual histology as a gold standard comparator, characterisation of plaques into soft, mixed and fibro-calcified has also been shown to be feasible by MSCT.[14] Even in occluded vessels such as CTOs, MSCT has been shown to be the best available alternative for characterisation of composition of the "missing segment".

Such features are important as the invasive angiographic equivalents have traditionally been associated with worse outcome with PCI

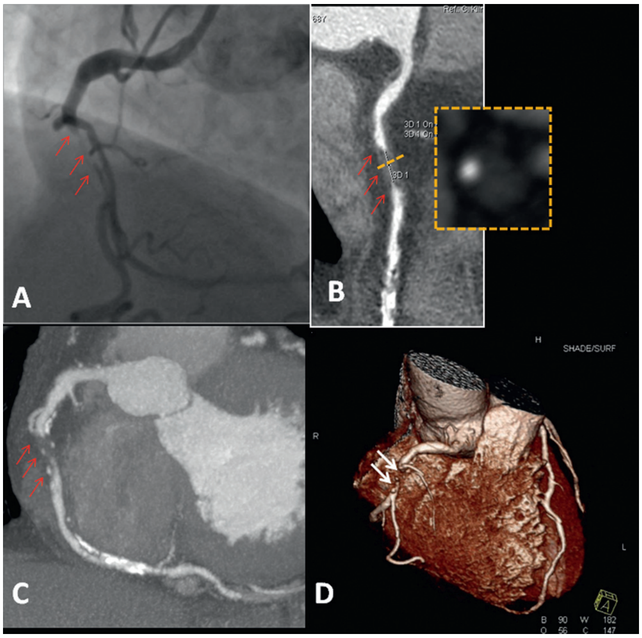

Figure 1. Chronic total occlusion of the right coronary artery. The invasive angiographic view (A), corresponding multiplanar reformation (B), maximum intensity projection (C), and volume rendered image (D). The segment of occlusion (red arrows) can be visualised in B and C. Specks of calcium can be appreciated in both B and C. The insert in panel B is a cross-sectional image showing calcium occupying <50% of the cross-sectional area, a feature associated with better chances of eventual PCI success. While the length of the segment is best measured from multiplanar reformation (B), volume rendering adds to the characterisation of the total occlusion by allowing better appreciation of the tortuosity and angles in space in 3-dimensions (D).

(Table 1). Indeed, calcification as determined by invasive angiography is associated with lower success rate of CTO-PCI.[3,12]

These observations, and the increasing utility and availability of cardiac MSCT, have inspired researchers to investigate whether MSCT is better than invasive angiography at characterising CTOs and predicting success of percutaneous intervention. Mollet et al were the first to point out the value of pre-procedural MSCT. Occlusion lengths of >15 mm and calcification involving >50% of a coronary wall on a cross-sectional image were independent predictors of procedural failure. Soon et al later explored the association between the degree of MSCT cross-sectional luminal calcification, as well as MSCT calcification length with the degree of CTO-PCI success in a small number of CTO lesions (n=43) with a 16-slice MSCT.[19] The degree of transluminal calcification was defined as the area of luminal calcification in relation to the total vessel cross-sectional area at the point in the occlusion showing the greatest extent of calcification. A more than 50% transluminal calcification was the only significant predictor of failed PCI in multivariable analysis. In fact, CTOs with ≥50% transluminal calcification were 10 times less likely to be treated successfully. MSCT calcification length measured as the sum of all lengths of calcified plaques in the occluded segment did not show association with PCI success, whereas CTO lesion length showed a weak association. This study confirmed that MSCT angiography is better

Table 1. Angiographic predictors of failure for percutaneous interventions on chronic total occlusions.

Moderate to severe calcification
Length of occluded segment of >15 mm
Blunt stump as opposed to tapered stump
Duration of ≥180 days
Tortuosity of proximal segment
Presence of antegrade bridging collaterals
Side branch at occlusion site
Absence of antegrade flow

at quantifying calcification in a CTO than conventional invasive angiography and added that the distribution of calcium within the lumen had a great impact on PCI success.

To better evaluate the best predictive characteristics of CTO calcification on PCI success, Cho et al[20] compared calcium volume, calcium concentration, calcium equivalent mass and calcium score and occlusion length from images acquired with a 64-slice CT in a group of 64 patients with 72 CTO lesions. All calcium parameters, except total calcium score (Agatston score), were higher in patients with procedural failure. The percentage cross-sectional calcium area was an independent predictor, confirming results by earlier studies. Additionally, a cut-off value of 53.86% was found to have excellent sensitivity and specificity to predict failure.

The site of calcification along the length of the lesion is also important. In fact, occurrence of calcification at the entry site of the occlusion as opposed to the exit site makes the antegrade approach of recanalisation more difficult.[10] This may be a reason for the tougher proximal fibrous cap of the CTO, and the increasing success rates of wiring the occlusion from the distal cap via collaterals in the retrograde approach.[21]

In a recent similar study, Ehara et al included calcification both on the inside and at either end of the occluded site with severe transluminal calcification quantified as high density plaques of >500 HU.[22] A 64-slice CT scanner was utilised in 110 patients with the same number of CTOs. Severe calcification was again an independent predictor of wiring success. The other CT derived morphological features that determined CTO-PCI success in this study were shrinkage and bending of the target vessel.

Shrinkage in the vessel, identified as abrupt narrowing or severe tapering of the distal portion to less than 1 mm in cross-sectional diameter, is probably an age-effect of the CTO. This may explain why the guidewire often tracks outside the vessel wall close to the distal cap, producing a perforation.

Bending, that is, an angle of >45 degrees in the trajectory of the vessel either in the occluded site or proximal vessel, was the most prominent predictor of the three morphological features. This finding is consistent with the previous invasive angiographic notions, that vessel tortuosity requires increased operator skill and experience. Moreover, the presence of bending and the trajectory of the “missing segment” can now be appreciated by MSCT. These four studies and the MSCT-derived parameters that showed predictive value for CTO-PCI success are summarised in Table 2.

Table 2. Studies that assessed the predictive value of multislice computed tomography (MSCT) – derived parameters.

	Mollet et al	Soon et al	Cho et al	Garcia-Garcia et al	Ehara et al
Scanner used	16-slice	16-slice	64-slice	16, 64-slice	64-slice
Patients	45	39	64	139	110
CTO lesions	47	43	72	142	110
Success rate	55%	56%	76%	62.7%	85%
MSCT characteristics associated with PCI-failure	Lesion length Ca.>50%CSA Blunt stump	Ca.≥50%CSA	Lesion length R Ca. volume R Ca. score R equivalent mass %Ca. area/CSA	Ca. at entry Ca.>50% CSA % angulation	Bending* Shrinkage* Severe Ca.*
Independent predictors	Ca.>50%CSA Lesion length Blunt stump		%Ca. area/CSA	Ca.>50%CSA	Bending Shrinkage Severe Ca.

CTO: chronic total occlusion; Ca.: calcium; Ca.>50%-CSA: percentage of calcium occupies more than half of the cross-sectional area at the point of maximum calcification in the occluded segment; R: regional; *see text for definition

The three dimensional nature of MSCT coronary angiography, appreciated best on the vessel reconstructions, has added value for vessel anatomy visualisation and lesion localisation which is superior to the invasive two dimensional angiography. Suboptimal projections with foreshortening, vessel overlap and problems with sizing from conventional invasive angiography often do not provide a clear picture needed to plan an interventional or surgical procedure on the coronary tree. CTOs occurring in left main or other ostial locations, or in patients with anomalous coronary arteries are better visualised by MSCT and are often better treated by bypass grafting.

Therefore, for planned PCI, pre-procedural MSCT of CTOs provides a roadmap. Devices can be selected according to the nature of the occluding plaque, that is either soft (lipid-rich) or hard (fibrocalcific). Moreover, the use of such images during the procedure itself can provide a visual landmark that can be used to steer the guidewire in the proper direction. The utilisation of intra-procedural MSCT data is a subject of much interest and is currently being explored.

Intra-procedural use of pre-acquired MSCT data

Invasive angiography images can be coupled in the offline MSCT workstation, allowing superimposition of MSCT data (Figure 2). To achieve accurate superimposition, the extracted coronary vessels of the MSCT have to be matched to the diastolic image of the invasive series using bifurcation points as markers. This compensates for respiration and other positioning differences. This superimposition allows the operator to visualise the trajectory and borders of the missing segment, and to localise the soft and calcified spots identified from the MSCT images in the invasive counterpart. A specific application is the use in ostial occlusion - which are most challenging on lumenography - and where MSCT overlay might be helpful. Initial software is limited to still frames, and a substantial amount of operator interaction is necessary. However, it has the potential to reduce the fluoroscopy time and contrast that would otherwise be necessary to regularly check the position of the guidewire in relation to the distal vessel. Also, in the long run this could eventually result in lower procedure times, however real-time and ECG-gated overlays will be necessary. This concept has also been applied to magnetic navigation in the catheterisation lab.

Magnetic navigation and MSCT

The ability of magnetic navigation technology developed by Stereotaxis, the Niobe® Magnetic Navigation System (Stereotaxis, Inc., St. Louis, MO, USA) to allow precise guidewire direction control is particularly attractive for CTO interventions.[23] The concept relies on two permanent external magnets situated at either side of the patient that can be rotated, translated or tilted to produce a uniform, magnetic field of 0.08 Tesla within the patient's chest. This field is used to precisely direct a tiny magnet mounted on the tip of a guidewire by changing its magnetic moments. This allows fine control of the orientation of the tip of the guidewire in space, achieving a full 360° omni-rotation.

For accurate vector changes by the magnets a virtual roadmap is necessary. In CTO lesions, this is ideally acquired from 3D volume-rendered images by MSCT. Extraction of the coronary tree from raw MSCT datasets on a software programme (Siemens Circulation™ Siemens AG, Munich, Germany) is followed by semi-automatic segmentation of the coronary tree. This post-processed data set is then imported into the Navigant® 2.11 software where centrelines, that is the trajectory in the middle of each vessel are computed. The pathway of the coronary vessel is automatically traced with manual assistance necessary in the occluded segment of the CTO[24] (Figure 3).

Co-registration of the MSCT data in the Navigant® software to two X-ray fluoroscopic images that are at least 30° apart and alignment of the centreline to the live fluoroscopy image is then performed. A touch screen monitor at the catheterisation table, within operating distance from the standing interventionalist, shows automatically updated images of the magnetic vector as the wire is advanced, as well as the corresponding endoluminal view and MPR slice (Figure 3). Additionally, a magnetically aided radiofrequency (RF) ablating wire can be guided through the occluded vessel.[24]

This technology has the potential to improve CTO-PCI. In our experience, application in interventions on complex lesions such as

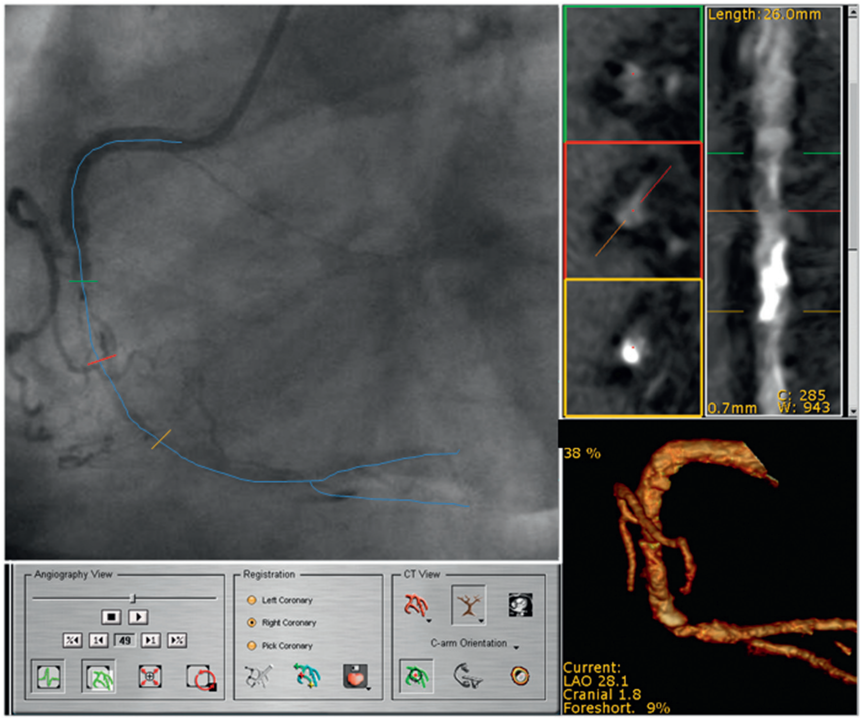

Figure 2. Multislice computed tomography with longitudinal, cross-sectional and 3D reconstruction all including the "missing segment" of the right coronary artery with a chronic total occlusion. Integration of such MSCT data onto live fluoroscopic images on software by Shina systems enables enhanced vessel characterisation. At each corresponding level along the vessel on the fluoroscopic image, the MSCT data provides additional information including plaque calcification, position and lesion length. Missing segment and distal segment visualisation provides a virtual "roadmap" and limits the need of control and contralateral contrast injections. (AngioCt; Shina Systems Ltd., Caesarea, Israel)

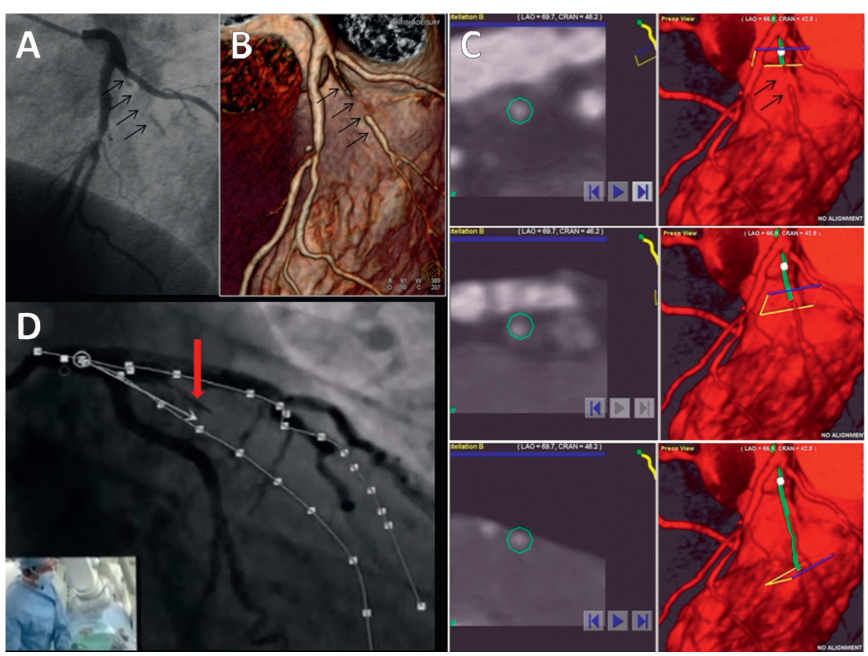

Figure 3. Three dimensional reconstruction (3DVR) on an offline work station is the first process required in preparation for magnetic-aided navigation. The missing segment and the proximal and distal stumps of the chronic total occlusion (black arrows) are better appreciated on 3DVR shown in panel B. A roadmap of total occlusion is created by importation of the MSCT data set into Navigant® and subsequently growing the proximal centreline along the occluded segment using cross-sectional multiplanar reconstruction (MPR) and volume rendered images (C, top to bottom) until the distal lumen is reached. The navigational centrelines with a directional vector can be visualised by co-registration onto live fluoroscopic images (D).

bifurcations, it provides enhanced safety and effectiveness with higher success rates and reduced contrast dose.[25,26] However, for use in CTO-PCI, preliminary results to date are somewhat disappointing. The main limitation is the ability to "steer" the wire through a totally occluded segment. The RF ablating wire should create sufficient space to redirect the tip if corrections are necessary.

Another important limitation is the static MSCT roadmap derived from diastole only. A dynamic 4D roadmap acquired from multiple phases during the cardiac cycle would improve accuracy and allow continuous co-integration. More importantly, the wire design with their "bulky" 2-3 mm tip is not ideal to be advanced through such tough obstructions.[24] These factors were considered the reason for the failure of improved success in tackling PCI-CTO using this combined technology. Major X-ray vendors are presently developing MSCT integration with the goal of creating 4D roadmaps. At present, 3D MSCT mapping from these vendors already allows this application in the lab and needs minimal user input with a few clicks (Figure 4). Integration of 4D MSCT data is in development, and achievable off-line for a single respiratory phase (Figure 5). To achieve respiratory gating, dedicated sensors using small magnetic fields such as those employed in the MPS-system from Mediguide (Haifa, Israel) have been developed and have to be integrated.[27]

Realistic current and potential future applications

Although of unproven benefit, pre-procedural MSCT images of the CTO in patients in whom this is the initial diagnostic test can be used as additional information throughout the patient management process as outlined below.

Planning the procedure

The availability of detailed anatomical information of the coronary arteries before intervention is essential. This allows more time for a meticulous consideration and discussion of the treatment options and/or best treatment strategy with the heart team consisting of an interventional cardiologist and a cardiac surgeon. The patient and hospital staff would be better prepared for handling an elective high risk procedure. Adequate pre-planning, as well as anticipation of possible complications, should lead to higher success rates and proper, timely management of any complications.

Wiring

Choosing the appropriate approach, that is, antegrade versus retrograde in cases where both are feasible (presence of good

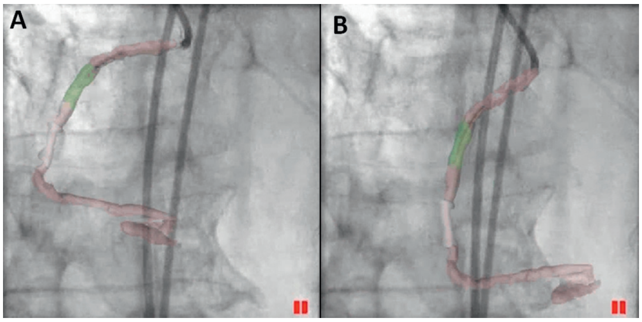

Figure 5. ECG-gated overlay with breathing correction. MSCT derived 3D reconstruction over-layed onto the fluoroscopic images with correction for breathing movements allows offline accurate superimposition of the two imaging modalities during end inspiration (panel A), and during end expiration (panel B).

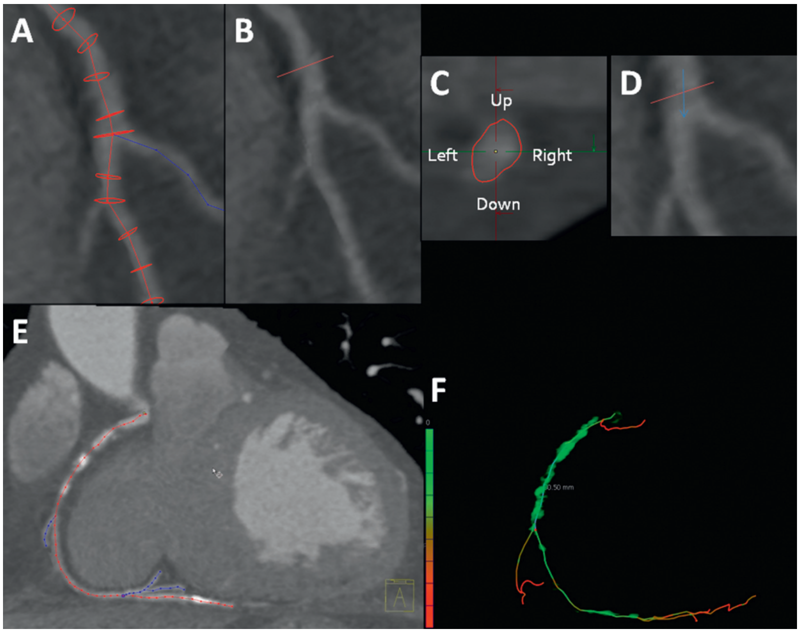

Figure 4. Integration of a linked-MSCT longitudinal view in such a way that it matches the real-time fluoroscopic view according to the C-arm position in the cathlab. Cross-sectional views can also be oriented appropriately with left-right and up-down positions as seen in panel A-D. The multiplanar reformation (E) is also synchronised to the C-arm. MSCT derived centreline, also coupled to the C-arm orientation, allows accurate length measurements vessel characterisation and choice of optimal fluoroscopic views (F) (CTO-guide; Siemens, Erlangen, Germany).

collaterals) can be accomplished based on the presence of calcification in the proximal fibrous cap of the CTO. Choice of wire - stiff, steerable, specialised wires- can be influenced by the presence and degree of calcification. Knowledge of the location of calcium can help us direct the wire away in order to avoid complications. The 3D reconstruction and superimposition, as well as synchronisation of gantry movements, can provide a visual aid and help optimise the projections, assessing the proper trajectory in the occluded segment. In magnetic navigation, the combination of optimal visualisation and control of the wire tip can be used to successfully cross CTOs, especially with the development of better magnetic wires.

Ballooning and use of debulking devices

The presence of calcium in the CTO plaque may necessitate higher balloon pressure inflations. For heavily calcified lesions, the need for additional lesion pre-treatment such as excimer laser use or rotablation can be anticipated.

Stent deployment

Appropriate stent sizing by MSCT, especially for CTO obstruction length, can lead to less stent overlap, the need of which may be associated with both acute complications such as dissections and perforation as well as long term complications of in-stent restenosis. The presence of plaque at the planned landing zones of the stent can be appreciated pre-procedurally on MSCT, and this can also potentially minimise the periprocedural complications as well as the occurrence of in-segment stenosis in the long term.

Follow-up

In-stent restenosis assessment by MSCT has been shown to be feasible. In the early days, with 16-slice MSCT scanners, only left main coronary stents could accurately be assessed. With the current 64-slice scanners, a larger cohort of stents can be investigated with a limited number of non-interpretable images where sensitivity and specificity are both 91%. However, it still gives higher false positives for smaller sized stents (≤2.75 mm).[28-30]

Complimentary or competing imaging for CTO

Alternative, non-invasive imaging techniques, such as cardiac magnetic resonance (CMR) are currently inferior to MSCT in providing detailed anatomical information of the coronary arteries that may be useful for CTO intervention. However, such imaging modalities, including contrast-enhanced CMR, positron emission tomography (PET)/CT and stress echocardiography, offer better and safer myocardial viability assessment which is often desirable information that may be useful in the choice of treatment strategy for CTOs.[6] Functional imaging using MSCT is still in its infancy, but appealing. Further development of technology, protocols and techniques for perfusion assessment by MSCT with delayed scans is underway and will be clinically available.[31]

CTO-PCI intra-procedural imaging is still dominated by invasive angiography despite its many limitations. Wire progression can be monitored in real-time by fluoroscopy, and timely contrast injections including contralateral ones allow early identification of complications. Its unsurpassed temporal (5-20 ms) and spatial (0.2 mm) resolution is particularly important in the often complex treatment strategies employed for CTO treatment. The benefits experienced by co-registration of pre-acquired MSCT and 2D fluoroscopy is a reality as pointed out earlier. Novel C-arm CT technology, with the use of flat panel detectors integrated in the C-arm at the catheterisation lab, has recently been introduced. Image acquisition and reconstruction are similar in principle to traditional MSCT with the added benefit of being acquired in the catheterisation lab and without the need of patient transfer. The potential of such innovative technology is substantial, but further development and advances are needed.[16] Since most of the difficulties in CTO treatment lies in wire penetration of the fibrous cap, the application of invasive imaging techniques, including IVUS and optical coherence tomography (OCT), is limited. IVUS can reliably identify the true lumen when the wire is sub-intimal. Once the lesion is successfully wired, IVUS with its "deep" penetration can assess plaque size and calcium content, while OCT, with its high resolution (10-15 µm) can identify dissection flaps and thrombus and can guide the choice of stent size and assess proper stent expansion.

Limitations

It is clear that MSCT can assess the anatomical features predictive of CTO-PCI failure better than conventional angiography.[10] This can lead to better case selection and, by restricting CTO-PCI attempts to those patients without unfavourable features, the success rates of CTO-PCI is likely to increase. However, this would mean that all patients who have a diagnosis of CTO have to undergo MSCT, if this was not the initial diagnostic test. The need of additional radiation and contrast-based imaging techniques in a patient whose eventual percutaneous procedure is already known to be associated with high doses of both, has to be evaluated. Using modern MSCT scanners, the estimated radiation dose reaches 8.5 to 12.5 mSv for cardiac scans, and although new scanning techniques such as "tube current modulation" and prospective gating, can reduce the dose further to 3-6 mSv without impacting diagnostic quality, this is still excessive exposure with an associated life-time risk of cancer of 0.22%. If the patient would then undergo PCI, an additional 39 mSv could be acquired. Additionally, the contrast dose of 75 ml for the scan and 455 ml during the PCI procedure puts the patient at a considerable risk of nephropathy.[10] The risk/benefit balance has to be therefore carefully examined and discussed with the patient.

Conclusion

MSCT coronary angiography reveals the anatomy of chronic total occlusions and offers predictive value for the success rate of these high risk coronary interventions. Its incremental value over conventional angiography in this respect allows better risk evaluation that should lead to an informed choice of the best treatment option for the patient. Although the better visualisation and understanding of the anatomical features of an occluded vessel can modify or optimise our intentional treatment strategy, more data is needed before MSCT is recommended routinely in patients with a CTO.

Further development in co-registration techniques for applications of MSCT intra-procedurally may, in the future, provide a tangible incremental value to this rapidly evolving technology.

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