Curr Cardiovasc Imaging Rep (2014) 7:9275
DOI 10.1007/s12410-014-9275-z

Cardiac CT and Stent Imaging: Update 2014

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Published online: 15 June 2014

Abstract Percutaneous coronary intervention with stent implantation is a common technique for coronary revascularization. Despite the widespread use of drug-eluting stents in-stent restenosis (ISR) is still a major issue. Multidetector row computed tomography angiography of the coronary arteries is a well-established, noninvasive tool for the assessment of the coronary arteries. Stent imaging, however, is a challenging task with relevant rates of nondiagnostic scans due to motion and beam-hardening artifacts. Nevertheless, recent scanners provide excellent results for the exclusion of ISR with a negative predictive value of about 97 %. Further indications for CT imaging of coronary stents include the detection and visualization of stent-related complications such as stent fracture. During the last couple of years there have been some major advances in CT imaging of coronary stents relating to hardware and imaging protocols. This review describes recent advances in CT imaging of coronary stents and summarizes current results

Keywords Computed tomography · Heart · Coronary artery disease · Stent · Revascularization therapy

Introduction

Percutaneous coronary intervention (PCI) with stent implantation is the most commonly used technique for coronary revascularization with about 492,000 procedures per year in the US and 854,000 in Europe [1, 2]. Although drug-eluting stents are nowadays used in the vast majority of procedures, in-stent restenosis (ISR) is still an issue of vital importance.

Downstream testing after PCI is commonly performed in order to exclude myocardial ischemia. While most patients undergo stress testing, a relevant number of patients undergo repeat invasive cardiac catheterization. The latter is known to be associated with major complications in about 2 % of procedures [3, 4]. Multidetector row computed tomography (MDCT) angiography of the coronary arteries is a well-established, noninvasive tool for the assessment of the coronary arteries. It is known to have an excellent negative predictive value (NPV) for the exclusion of coronary artery disease (CAD). However, there are several groups of patients, including patients with coronary stents, who are considered difficult to image [5]. Based on studies with 4-slice and 16-slice CT, CT imaging of coronary stents was generally discouraged. With the introduction of 64-slice CT scanners, imaging of coronary stents has gained more acceptance due to their better spatial and temporal resolution leading to improved image quality. However, it is still a challenging task with relevant rates of nondiagnostic examinations as a result of motion and beam-hardening artifacts.

General technical considerations and common strategies for image assessment have previously been reviewed in this journal [6]. Since then several technical and clinical developments have further strengthened the role of MDCT in the work-up of patients after PCI. This article reviews this new evidence in CT imaging of coronary artery stents.

Technical Innovations

New Hardware

Within the last few years there have been some relevant improvements in CT scanner hardware, which are relevant to

This article is part of the Topical Collection on *Cardiac Computed Tomography*

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coronary CT imaging and the assessment of coronary stents in particular. With the most recent introduction of third-generation dual source CT (DSCT) into clinical routine practice, temporal resolution has been brought down to 66 ms. It can be further reduced by multisegment image reconstruction algorithms. The latter approach, however, suffers from several shortcomings such as higher radiation exposure and potential spatial inaccuracies, as data from several heart beats are used to compute the actual image.

Most recent CT scanners provide tube voltages from 70 kV up to 150 kV in contrast to the previous generation of scanners, which mostly provided 100 kV to 140 kV. Although the use of DSCT has not yet been tested with coronary stents, it might be useful in reducing beam hardening artifacts at the cost of higher radiation exposure than with low tube voltages down to 80 kV. The availability of a broader range of tube voltage settings is likely to improve dual energy CT imaging. The latter is an interesting approach to the imaging of coronary stents, as dual energy imaging with monoenergetic image reconstruction can reduce metal artifacts [7].

Another interesting new hardware development is the introduction of new detector technology, in which a photodiode and analog-to-digital converter are integrated in a single application-specific integrated circuit directly attached to the ceramic scintillator, thereby reducing the number of separate detector components. Consequently the number and lengths of electric circuit paths are reduced, which minimizes the electronic noise and crosstalk between the detector channels. In theory this should result in reduced image noise and slightly improved spatial resolution. In coronary CT angiography this new detector design has been shown to reduce image noise and improve stenosis quantification [8]. In CT imaging of coronary stents its key advantage is a significantly reduced image noise [9]. With stents being routinely imaged using sharp and therefore noisier convolution kernels, this is an important achievement. It can be used either to further reduce radiation exposure or to improve lesion conspicuity by better lesion delineation. The latter, however, has not yet been shown in clinical routine practice. Besides, even with the most recent scanner and image reconstruction techniques about 1.8–1.9 mm of a coronary stent lumen are not sufficiently accessible [9]. This problem is independent of the available scanner platform, with the type and size of stent having the biggest impact on the visibility of the stent lumen [10]. As a consequence stents with a diameter of ≤3 mm are still not suited to routine CT imaging [10, 11].

Image Reconstruction

The most relevant technical achievement in CT imaging of coronary stents originates from a new image reconstruction technique. Iterative image reconstruction has become routine in CT imaging of coronary stents. This approach has been established by all vendors and is independent of the type of scanner. In in vitro studies the image noise is reduced by a factor 2–3 using iterative reconstruction techniques, when compared to standard filtered backprojection (FBP) [9, 11]. This finding has been confirmed in head to head comparisons in routine clinical practice [12, 13]. Moreover, recent studies indicate that the use of iterative reconstruction techniques improves diagnostic accuracy [14–16]. The advantage of iterative image reconstruction in terms of better signal-to-noise ratios persists even if the tube current–time product is reduced by 50 %, allowing further improvements in terms of radiation exposure [13]. Across different vendors the use of higher iterative reconstruction settings, i.e. more iterations, appears to be particularly beneficial for CT imaging of coronary stents (Fig. 1) [11, 16]. However, there are differences in detail among the different vendors as the technology and implementation of iterative image reconstruction vary widely.

Scanning Protocols

Two key issues in the CT imaging of coronary stents are the assessment of small stents with a diameter <3 mm and concerns regarding radiation exposure with the increasing use of cardiac CT. Both issues are addressed with advanced scanning protocols. As known from coronary CT angiography for the exclusion of CAD, sequential scan modes and recently introduced prospectively ECG-triggered high pitch scanning are effective ways to reduce radiation exposure (Tables 1 and 2). The latter even permits coronary CT angiography with a total radiation exposure of less than 1 mSv. Only recently a prospective study evaluated this technique for the imaging of coronary artery stents. In direct comparison with established scanning protocols there were no differences in diagnostic accuracy, while the radiation dose was brought down from 13±3.4 mSv for spiral scanning with retrospective ECG gating to 3±1.4 mSv for sequential and 1±0.5 mSv for high pitch scanning [17]. Using low tube voltage settings of 80 kV and additional iterative image reconstruction even permits CT imaging of coronary stents with a radiation exposure at submillisievert levels and good diagnostic results [15].

Direct visualization of the coronary stent lumen is particularly limited in small stents or in the presence of motion artifacts. Consequently a relevant number of stents cannot be evaluated (Tables 1 and 2). In earlier studies with 16-slice CT, indirect parameters such as the difference in attenuation between the reference lumen proximal to the stent and and the in-stent lumen were applied [18]. From theory the best indirect parameter for detecting ISR is myocardial ischemia, as this not only indicates potential ISR, but also provides functional information on the need to treat. The combination of CT angiography and stress perfusion imaging is an elegant way to provide morphological and functional information in a

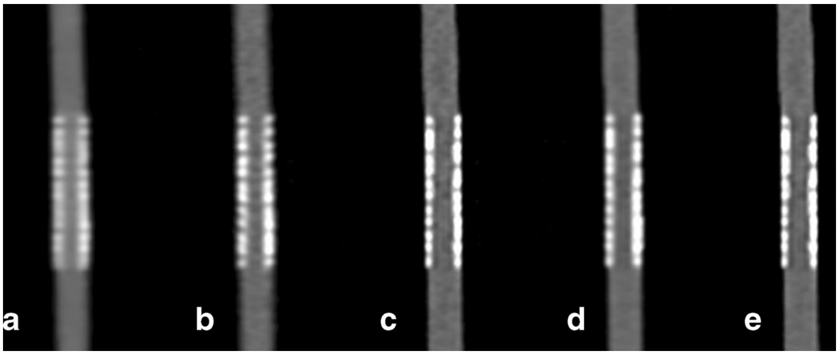

Fig. 1 Comparison of different reconstruction techniques applied to the same raw data from a 3.5-mm bare metal stent (PRO-Kinetic; BIOTRONIK, Berlin, Germany). Data were obtained with the most recent generation of dual source CT scanner with an application-specific integrated circuit attached to the ceramic scintillator. From left to right FBP with a medium smooth standard reconstruction kernel (**a**), FBP with a sharp kernel (**b**), fourth generation iterative reconstruction (**c**–**e**) with the same sharp kernel (**c**) and an ultrasharp kernel (**d**) each using a medium strong level of iterations and an ultrasharp kernel at a high level of iterations (**e**). Applying iterative reconstruction, the image noise is brought down and even ultrasharp reconstruction kernels can be used at acceptable noise levels allowing detailed assessment of most of the stent lumen

single procedure. This idea was applied by Magalhaes et al. in 2011 [19] and has only recently been confirmed in a multicenter study [20••]. While stress testing alone was inferior to CT angiography it was found to be useful in patients otherwise excluded due to inaccessible stented segments. Combined evaluation by CT angiography and CT perfusion imaging markedly improves diagnostic accuracy. Interestingly, the radiation exposure with this method was lower than in invasive catheter angiography (7.9±2.8 vs. 9.5±5.1 mSv), despite the need for repeated CT scans [20••]. Thus this technique is likely to become more relevant in the near future. The combination with prospectively ECG-triggered high pitch scanning offers the potential to use this approach at radiation levels comparable to 1 year of background radiation, which appears to be reasonable for diagnostic purposes in patients with known CAD and a history of PCI.

Evidence and Recommendations in ISR

Despite relevant improvements in scanner hardware and reconstruction techniques, phantom studies still indicate important limitations of CT imaging of coronary stents with artificial lumen narrowing in the range 35 % to 60 % depending on the type of stent [11]. In general smaller stents show more pronounced artificial lumen narrowing [10].

While these phantom data appear to be discouraging, the clinical findings are more encouraging. Three meta-analyses on the value of 64-slice CT imaging in coronary stents have shown encouraging results for the use of MDCT in the imaging of coronary stents [21–23]. The overall sensitivity, specificity, positive predictive value (PPV) and NPV for assessable stents reported by Kumbhani et al. were 91 %, 91 %, 68 % and 98 % [23]. With recent DSCT and ≥256-slice CT scanners the results are comparable with NPVs in the range 95 – 100 % (Table 2). Only lately has CT also been shown to be capable of classifying ISR according to its morphology on the basis of the prognostically relevant Mehran classification [24]. Most recent data using iterative reconstruction techniques, however, indicate better sensitivity and higher NPVs at the cost of lower specificity and PPV (Table 2). In part this might be due to a decrease in the number of stents excluded from analysis, which decreased from an average of 14 % with 16-slice CT [25] to 10 % with state of the art scanners. Another, probably more relevant factor might be a different interpretation pattern, where higher sensitivities are obtained at the cost of lower specificities. The low PPV is of concern as with the decreasing rate of ISR there may be an increasing number of false-positive findings, potentially leading to additional downstream testing. However, this particular issue has not yet been investigated.

Interpretation of the data is still controversial. Two of the meta-analyses on 64-slice CT were based on identical sets of clinical studies, but came to different conclusions. While Sun et al. consider 64-slice CT to be an alternative to conventional coronary angiography [22], Kumbhani et al. conclude that stress imaging remains the most acceptable noninvasive technique for diagnosing ISR [23]. The latter interpretation is supported by a recent analysis of Medicare data for the period 2005 – 2007, which indicated a higher rate of downstream testing in patients undergoing coronary CT angiography after PCI [26]. However, while this is an interesting and clinically relevant approach, one has to be aware that the data base were obtained almost a decade ago and CT provides better results for detecting ISR than other noninvasive diagnostic tests including myocardial SPECT [27, 28]. Moreover, new scanning protocols include CT angiography and stress CT perfusion [19, 20••]. Thus cardiac CT is gaining ground for ruling out significant ISR.

Table 1 Summary of studies on the diagnostic performance of 64-MDCT and 64-DSCT for detecting ISR published since 2010

Reference	Year	Scanner	No. of patients	No. of stents	Nonevaluable (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Dose (mSv), mean ± SD
[46]	2010	64-MDCT	93	140	14	27	95	67	78	n.a.
[47]	2010	64-MDCT	26	42	20	97	100	97	100	n.a.
[48]	2010	64-MDCT	55	122	13.2	91	95	96	91	n.a.
[49]	2010	64-MDCT	60	91	24.2	90	74	58	95	n.a.
[50]	2011	64-MDCT LPS	85	163	5	86	97	91	96	18.5±5.5
		64-MDCT SEQ	83	174	7	94	100	100	98	4.3±1.4
[51]	2011	64-MDCT	18	29	0	100	95	89	100	n.a.
[19]	2011	64-MDCT CTA	46	n.a.	21	85	77	87	74	15.9±4.8
		64-MDCT CTA/CTP		n.a.	0	88	95	97	81	
[52]	2011	64-DSCT LPS	30	56	12.5	94	87	77	97	14.6±3.3
		64-DSCT SEQ	30	59	13.6	100	84	68	100	2.2±0.5
[53]	2011	64-DSCT	34	34	0	100	74	18	100	n.a.
[54]	2012	64-MDCT	83	171	28.7	100	69	25	100	9.4±0.8
[55]	2012	64-DSCT	50	115	0	69.2	91.2	50	95.9	10.8±2.9
[56]	2012	64-DSCT	24	24	0	89	68	32	97	n.a.
[34•]	2013	64-DSCT	150	221	3.6	83.3	93.8	66.7	97.4	n.a.
[24]	2013	64-MDCT	61	101	0	100	75	92.45	100	9.4±0.9
			928	1542	Mean ± SD 9.6±9.6	Mean ± SD 87.9±17.7	Mean ± SD 86.5±11.3	Mean ± SD 71.2±26.7	Mean ± SD 94.1±8.3	

CTA CT angiography, *CTA/CTP* CT angiography combined with CT perfusion, *LPS* retrospectively ECG-gated low pitch scan, *n.a.* not available, *SEQ* prospectively ECG-triggered sequential scan

Table 2 Summary of studies on the diagnostic performance of ≥256-MDCT and 128-DSCT for detecting ISR

Reference	Year	Scanner	No. of patients	No. of stents	Nonevaluable (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Dose (mSv), mean±SD
[57]	2010	320-MDCT	53	89	8	92	83	46	98	7.1±1.7
[15]	2013	128-DSCT FBP	50	87	30	97	53	80	90	0.32
		128-DSCT IR			25.0	100.0	65.0	85.0	100.0	
[17]	2013	128-DSCT HPS	55	80	0	100.0	97.1	83.3	100.0	1.0±0.5
		128-DSCT LPS	65	90	0.0	90	97.1	81.8	98.6	13.0±5.4
		128-DSCT SEQ	60	86	0.0	93.3	97.3	87.5	98.6	3.0±1.4
[14]	2013	256-MDCT STD	28	28	0	83.3	50	33.3	91.6	12.1
		256-MDCT HR			0	100	29.6	40	100	
		256-MDCT IR			0	100	54.5	40	100	
[20••]	2013	320-MDCT CTA	91	221	22	59	74	77	95	3.0±1.8
		320-MDCT CTP			1	65	69	33	90	4.9±1.9
		320-MDCT CTA/CTP			0	82	88	61	96	7.9±2.8
[16]	2013	128-DSCT FBP	42	73	27	83	71	36	96	0.32±0.02
		128-DSCT IR			27	100	76	44	100	
			Total 444	Total 754	Mean ± SD 10.0±12.8	Mean ± SD 88.9±13.3	Mean ± SD 71.8±20.2	Mean ± SD 59.1±22.1	Mean ± SD 96.7±3.8	

CTA CT angiography, *CTP* CT perfusion, *CTA*/*CTP* CT angiography combined with CT perfusion, *FBP* filtered backprojection, *HR* high-resolution kernel, *IR* iterative reconstruction, *LPS* retrospectively ECG-gated low pitch scan, *SEQ* prospectively ECG-triggered sequential scan, *STD* standard soft kernel

Current recommendations on the use of cardiac CT for stent imaging follow a conservative approach. The "Appropriate Use Criteria for Cardiac Computed Tomography" were last revised in 2010 with CT imaging of coronary stents being considered appropriate in a few indications such as risk assessment in asymptomatic patients after PCI with left main coronary artery stenting and a stent diameter ≥3 mm [29]. Accordingly the 2010 expert consensus on the use of cardiac CT considered 64-slice CT a potentially reasonable alternative to invasive angiography to rule out significant ISR in patients with low-to-intermediate probability of restenosis [30]. Most recent major German consensus recommendations on the use of cardiac imaging with computed tomography and magnetic resonance imaging consider the use of CT for assessing ISR after PCI as not sufficiently robust. As a consequence this particular indication is rated "uncertain" [31].

These recommendations were based on evidence gathered with the use of 64-slice coronary CT angiography. The further improvements achieved with DSCT and ≥256-slice CT are not yet reflected in these guidelines. Moreover, economic parameters and patient preferences need to be considered. While patients typically prefer the less invasive test over invasive catheter angiography, coronary CT angiography is often cheaper and readily available almost without any patient preparation [32, 33]. As a consequence the current guidelines on the appropriate use of coronary CT angiography in the presence of coronary stents need to revised in the near future.

Clinical Applications Beyond ISR

CT imaging of coronary stents may not only permit the detection ISR but may also be suitable for estimating an individual patient's prognosis. Until recently this aspect has not been investigated for coronary stent imaging. An initial retrospective study indicated a strong relationship between the presence of ISR as seen on CT and major adverse cardiac events (MACE). Patients without ISR on MDCT had a low event rate of 4.8 %, while patients with ISR on MDCT had an event rate of 44.4 %. Patients with ISR <50 % had significantly lower MACE rate than patients with obstructive ISR >50 %. Correspondingly, over a 2-year follow-up period, 94±3.2 % of patients without ISR, 79±11.4 % of patients with <50 % ISR and 43±9.7 % of patients with obstructive ISR >50 % were free from MACE [34•]. This graded relationship between MACE and ISR provides a worthwhile basis for further investigations on the value of CT for assessing an individual patient's prognosis after PCI. Moreover, the recently introduced application of Mehrans classification to cardiac CT may provide another approach to assessing an individual patient's prognosis after PCI [24].

Coronary CT angiography is also used for assessing complications after stent placement. With the increasing use of drug-eluting coronary stents, stent-related pseudoaneurysms are more commonly reported. According to anecdotal evidence, these pseudoaneurysms can be identified by CT [35]. For several years, a limited number of experimental studies and studies in small patient series have investigated the use of CT imaging of coronary stents for evaluating stent-related complications, namely stent fracture (Fig. 2) [36]. This is of interest as stent fractures are known to lead to cause ISR [37], the development of pseudoaneurysms [38], embolization of stent material [39], and stent thrombosis [40]. Moreover, stent fracture is potentially an important factor in assessing an individual patient's prognosis. In a most recent study stent fracture of sirolimus-eluting stents as identified on CT angiography was identified as a significant risk factor for target lesion revascularization and MACE (hazard ratio 5.36, $p<0.01$) [41].

Future Directions

In the near future two major developments will further enhance the clinical value of CT imaging of coronary stents: improved visualization techniques and new clinical indications.

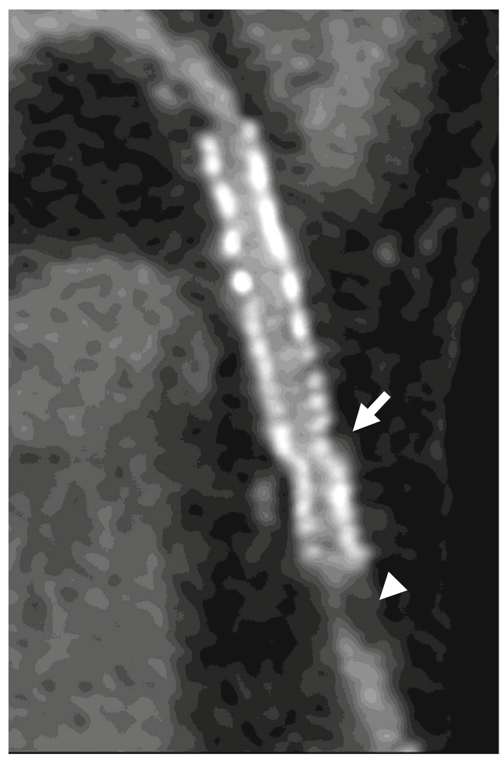

Fig. 2 CT coronary angiogram obtained from 68-year-old symptomatic patient 2 years after implantation of a bare metal stent in the right coronary artery. Curved reformatting shows a step in the stent distally indicating stent fracture (*arrow*) and an atheromatous plaque distal to the stent (*arrowhead*) causing a hemodynamically relevant stenosis

Technical improvements are likely to be incremental with further improvements in scanner hardware. The most recent generation of DSCT scanners provides a temporal resolution of 66 ms with a collimation of 0.5 mm. More interesting are new imaging concepts combining morphological and functional aspects. Within the last 2 years CT perfusion has become increasingly used for assessing the functional impact of ISR. The combination of CT angiography and CT perfusion is likely to become more and more important in the imaging of stents where direct visualization of the stent lumen will remain an unresolved challenge for the foreseeable future. Another development will be a more quantitative approach to ISR. This will include techniques such as coronary opacification gradient analysis, as this approach has been introduced in conventional coronary CT angiography [42, 43].

New indications will include the follow-up of patients in clinical studies. With coronary CT angiography becoming increasingly reliable for assessing coronary stents there might be a niche for noninvasive imaging. The value of CT has already been proven in two studies testing new resorbable drug-eluting scaffolds, namely the ABSORB and the DESolve trials [44, 45]. In both studies CT was one of the imaging endpoints. CT can be used in the setting of resorbable scaffolds since no blooming or streak metal artifacts are produced as are seen with metal-based stents.

Conclusion

Although stent imaging has been possible ever since cardiac CT was introduced into clinical routine practice, its use is still limited. Within the last couple of years major technical improvements have paved the way for more widespread clinical use. Its value for assessing an individual patient's prognosis has only recently been recognized and new indications such as for follow-up in clinical trials and assessment of complications are not fully developed. Nevertheless, the use of CT in the imaging of coronary stents with a diameter of <3 mm is still limited and knowledge on the size and type of stents is needed to achieve acceptable results. Considering the most recent developments including functional imaging, current guidelines on the use of CT imaging of coronary stents need to be updated. In selected patients cardiac CT should be considered as an alternative to catheter-based coronary angiography in the presence of coronary stents.

Compliance with Ethics Guidelines

Conflict of Interest Andreas H. Mahnken declares no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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