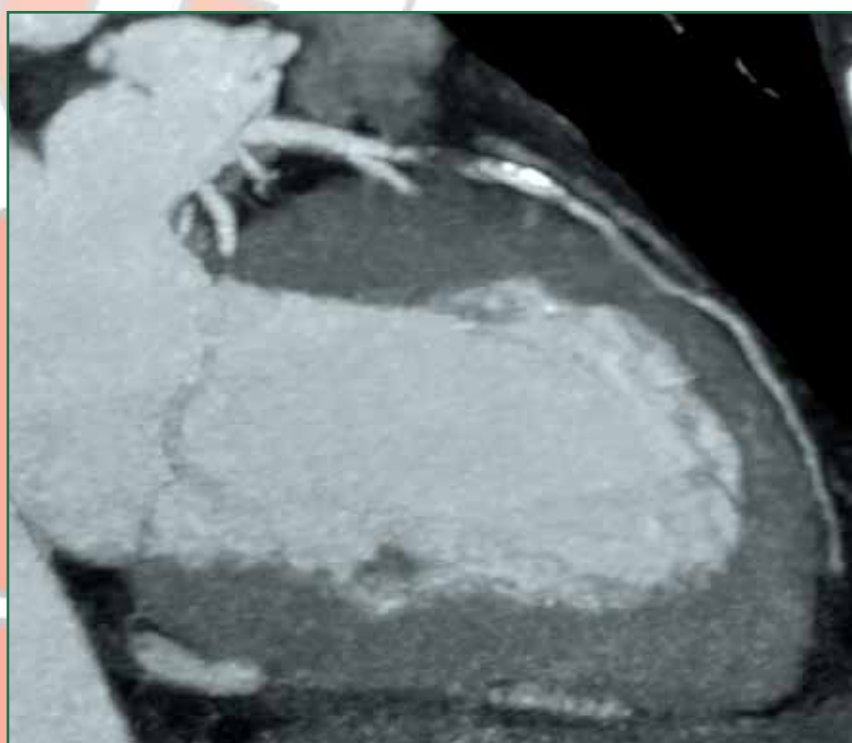


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Occlusion on mid left anterior descending (LAD) artery.

Koronarografija kompjutoriziranom tomografijom

Coronary computed tomography angiography

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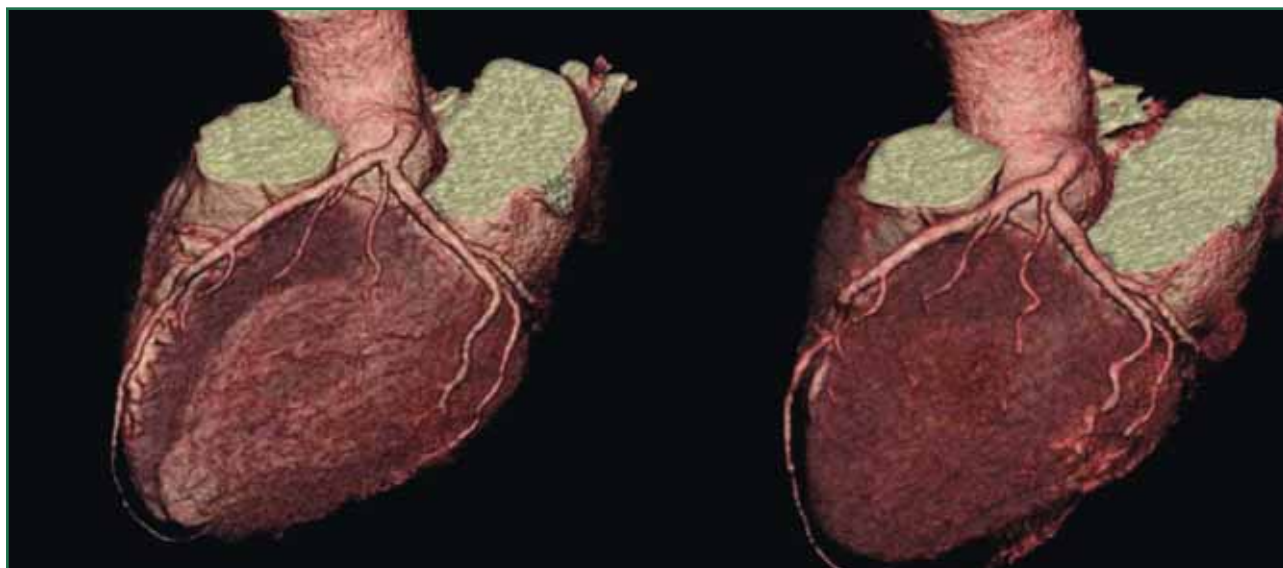
SAŽETAK: Cilj rada je prikazati najnovije kliničke dokaze o korisnosti koronarografije kompjutoriziranom tomografijom (MSCT koronarografija), ove još uvijek nove i kod nas nedovoljno etablirane metode, koja ima sve značajniju ulogu u dijagnostici koronarne bolesti srca (KBS). MSCT koronarografija predstavlja neinvazivnu dijagnostičku metodu za evaluaciju KBS s odličnim slikovnim prikazom i izvrsnom dijagnostičkom preciznošću koja je komparabilna s invazivnom koronarografijom koja se smatra zlatnim standardom u dijagnostici KBS.

KLJUČNE RIJEČI: MSCT koronarografija, koronarna bolest srca, neinvazivna kardiološka dijagnostika.

SUMMARY: The aim of the article is to present the latest clinical evidence of benefit of coronary computed tomography angiography (CCTA), which is still a new and insufficiently established method in our country which plays more and more important role in the diagnostics of coronary heart disease (CHD). CCTA represents a non-invasive diagnostic method for the evaluation of CHD with excellent image presentation and excellent diagnostic precision that is comparable with invasive coronary angiography that is considered a golden standard in the CHD diagnostics.

KEYWORDS: Coronary computed tomography angiography, coronary artery disease, noninvasive cardiac diagnostics.

CITATION: Kardio list. 2010;5(8-9):106-112.



Volume-rendering technique (VRT) presentation of functionally significant bridge on mid LAD artery.

Cilj ovog rada je prikazati kliničke dokaze o korisnosti, koronarografije kompjutoriziranom tomografijom (MSCT koronarografija) još uvijek nove i kod nas nedovoljno etablirane metode, koja ima sve značajniju ulogu u dijagnostici koronarne bolesti srca (KBS). Ova bolest predstavlja vodeći uzrok smrtnosti u većini razvijenih zemalja, a za pravovremeno i učinkovito liječenje KBS ključno je njeno rano otkrivanje. Tragičnu činjenicu predstavlja što je u 50-60% slučajeva, u do tada asimptomatskih bolesnika, prvi znak bolesti infarkt miokarda, a nerijetko i iznenadna srčana smrt¹⁻¹³.

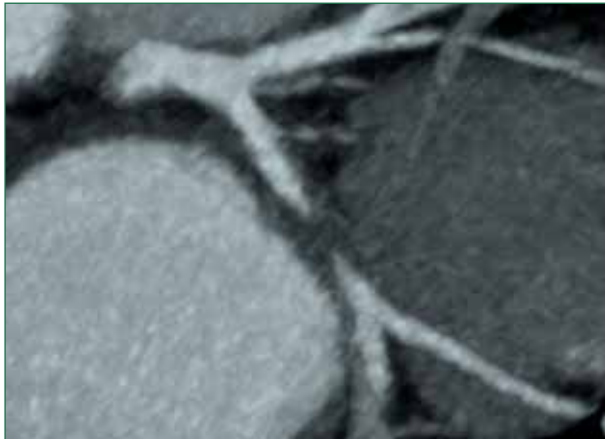
Temeljem analize podataka 398.978 pacijenata bez poznate KBS, uključenih u *American College of Cardiology National Cardiovascular Data Registry*, u kojih je učinjena elektivna koronarografija, značajni oblik KBS je potvrđen u samo u 38% slučajeva. Voditelji registra zaključu-

The aim of this article is to present clinical evidence of benefit of coronary computed tomography angiography (CCTA), which is still a new and insufficiently established method in our country which plays more and more important role in the diagnostics of coronary heart disease (CHD). This disease is a leading cause of mortality in the great number of developed countries, while early detection of CHD is crucial for timely and efficient treatment. The tragic fact is that in some 50-60% of cases in asymptomatic patients so far, the first sign of disease is the myocardial infarction, and usually a sudden cardiac death¹⁻¹³.

Based on data analyses of 398,978 patients without known CHD, included in *American College of Cardiology National Cardiovascular Data Registry*, for whom elective coronary angiography was made, the more important form of CHD was confirmed in only 38% of cases. The Registry leaders conclude that the current existing strategies for



ju da trenutno postojeće strategije za obradu pacijenata bez poznate KBS, a s postojećim rizikom, nisu zadovoljavajuće i potrebno ih je značajno unaprijediti⁴. Upravo ovdje vidimo najveću potencijalnu korist od MSCT koronarografije koja, ako se provodi na primjerenim uređajima i na primjeren način, može isključiti KBS s negativnom prediktivnom vrijednošću većom od 95%⁵ i na taj način mogu se izbjeći daljnja nepotrebna testiranja poput perfuzijske scintigrafije i invazivne kardiološke obrade koje imaju svoje rizike i komplikacije, a i značajno su skuplje od MSCT koronarografije.



A. Coronary computed tomography angiography: subtotal stenosis of left circumflex artery.

workup of patients without known CHD with the existing risk are not satisfactory and they need to be greatly improved⁴. This is where we see the greatest potential benefit from CCTA which, if conducted by using adequate devices and in an adequate manner, may exclude CHD with negative predictive value greater than 95%⁵ and this is how further unnecessary tests such as perfusion scintigraphy and invasive cardiac diagnostics may be avoided accompanied by their risks and complications, and they are much more expensive than CCTA.



B. Invasive coronary angiography: before percutaneous coronary intervention.

Postupak oslikavanja

Oslikavanje je potrebno vršiti na CT-uređajima posebno konstruiranim za snimanje srca i koronarnih arterija. Prema današnjim standardima radi se o uređajima s minimalno 64 uzastopna sloja oslikavanja. Jedino na ovakvim uređajima moguće je postići zadovoljavajuću kvalitetu snimke uz prihvatljivo nisku dozu zračenja. Uređaj također mora minimalno omogućavati i modulaciju intenziteta zračenja ovisno o EKG-u pacijenta te anatomske građi.

Frekvenciju rada srca je potrebno sniziti na maksimalno 65/min. Ukoliko pacijent ima višu frekvenciju tada se ordinira beta blokator *per os* ili češće parenteralno (Tenormin, amp. á 5 mg, doza lijeka se individualno prilagođava). Neposredno prije samog snimanja ordinira se i nitrat kratkog djelovanja sublingvalno (Nitrolingual spray) uz kontrolu krvnog tlaka. Ovo istovremeno omogućava korištenje protokola s malim dozama zračenja te maksimalno sužavanje područja oslikavanja u sve tri prostorne ravnine.

Također je potrebno jakost i napon struje na RTG-cijevi individualno prilagoditi svakom pacijentu obzirom na indeks tjelesne mase (BMI), opseg prsišta, frekvenciju i stabilnost rada srca.

Na ovaj način moguće je značajno smanjiti doze zračenja, koje kod uobičajene populacije mogu biti u razini 2-3 mSv, a kod idealnih pacijenata (BMI ≤ 25 , stabilna frekvencija ≤ 60 /min) i ispod 1 mSv⁶. Uporabom neprimjerenih uređaja te uz neprimjeren postupak oslikavanja, čak i na vrhunskim uređajima, doze zračenja mogu biti i višestruko veće.

Imaging procedure

Imaging is to be done on CT devices especially designed for imaging of heart and coronary arteries. According to the recent standards, these are the devices with minimum 64 consecutive imaging slices. This is the only device that may provide satisfactorily quality of the image with an acceptable low level of radiation. The device must minimally ensure modulation of the radiation intensity depending on patient's ECG and anatomical structure.

The heart rate needs to be lowered to maximum 65/min. If a patient has a higher rate, then beta blocker *per os* or more often parenterally are administered (Tenormin, amp. á 5 mg, medication dose is adjusted individually). Immediately prior to the imaging itself, nitrate with short effect is administered sublingually (Nitrolingual spray) thereby controlling blood pressure. This simultaneously enables using protocol with small radiation doses and maximum reduction of imaging area in all three spatial plains.

Strong current and voltage in X-ray pipes need to be individually adjusted for every patient considering the body mass index (BMI), thorax range, and heart beat rate and stability.

In this way it is possible to greatly reduce the radiation doses that in ordinary population may be at the level 2-3 mSv, and in ideal patients (BMI ≤ 25 , stabile heart rate ≤ 60 /min) and below 1 mSv⁶. The use of inappropriate devices and application of inappropriate imaging procedure even on top quality devices may lead to radiation doses higher by several times.



U svakodnevnom radu primjenjuju se preporuke *American Heart Association* te *International Commission on Radiation Protection* poznatije kao ALARA (As Low As Reasonably Achievable) protokol⁷.

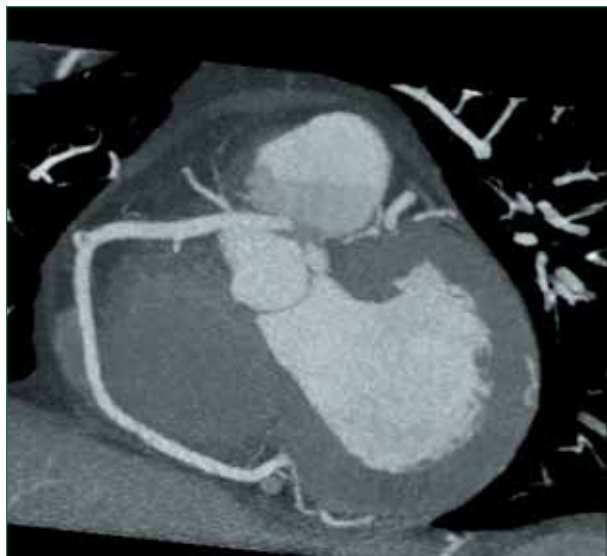
Nakon rapidnog tehnološkog razvoja u posljednjem desetljeću MSCT koronarografija je dokazano najpreciznija neinvazivna slikovna tehnika koja s 99% preciznošću može isključiti KBS. Danas se primjenjuje u više od 2.000 centara samo u Sjedinjenim Američkim Državama i pokrivena je zdravstvenim osiguranjem u svih 50 država. Metoda se sve više primjenjuje i u ostalim zemljama diljem svijeta, a od 2007. godine i u Republici Hrvatskoj. U Poliklinici Sunce u Zagrebu od ožujka 2007. do sredine 2010. godine učinjeno je više od 3.000 MSCT koronarografija, a klinička zapažanja i iskustva podudaraju se s navedenim *evidence-based* rezultatima⁸.

Razvojem CT uređaja sa 64 i više slojeva, posebno konstruiranih za oslikavanje srca, MSCT koronarografija je vrlo brzo postala etablirana metoda u oslikavanju koronarnih arterija, a kod sumnje na prirodenu anomaliju koronarnih arterija i metoda izbora.

In routine daily work, the recommendations by the American Heart Association and International Commission on Radiation Protection known as ALARA (As Low As Reasonably Achievable) protocols are used.⁷

Following the rapid technologic development during the last decade, CCTA is proved to be the most precise noninvasive imaging technique that with 99% precision may exclude CHD. Today it is used in more than 2,000 centers only in the United States of America and it is covered by health insurance in all 50 states. The method is more and more applied in other countries all over the world and since 2007 it has been applied in Croatia as well. More than 3,000 CCTA were conducted from March 2007 till mid 2010 in the Sunce Polyclinic in Zagreb, while clinical observations and experience overlap with the aforementioned *evidence-based* results⁸.

With development of CT device with 64 slices and more than that, especially created for imaging the heart, CCTA has soon become a very established method in imaging coronary arteries and in case of suspecting congenital anomaly of coronary arteries it has become a method of choice.



The anomalous starting point of the right coronary artery (RCA) from the left main coronary artery. RCA passes between the aorta and artery pulmonalis which may be dangerous for life.



Indikacije za MSCT koronarografiju

Indikacije za MSCT koronarografiju^{9,10}:

- Bol u prsima kod pacijenta s intermedijarnim rizikom
- Dvojbena rezultata stres testa
- Anomalije koronarnih arterija
- Evaluacija kardiomiopatije
- Preoperativna obrada kod nekoronarnih kardijalnih operacija

• Suspektna patologija aorte ili plućne arterije

• Prije i posle elektrofizioloških ispitivanja.

Novije indikacije su vezane su uz 64-slojni CT:

• Evaluacija boli u prsima ili zaduhe kod pacijenta s prethodnim aortokoronarnim premoštenjem ili implantacijom stenta

• Evaluacija akutne boli u prsima u hitnoj službi.

Temeljna uloga MSCT koronarografije, zbog njene visoke negativne prediktivne vrijednosti, je isključenje značajne koronarne bolesti srca kod simptomatskih pacijenata s niskim ili srednjim rizikom. Pacijenti s tipičnom kliničkom slikom i visokim rizikom za koronarnu bolest s jasno pozitivnim testom opterećenja imaju indikaciju za invazivnu koronarografiju. Primjena MSCT koronarografije kod asimptomatskih pacijenata se ne preporuča.

Današnji uređaji imaju temporalnu rezoluciju ≤ 150 msec što uz submilimetarsku prostornu rezoluciju omogućava vjeran prikaz koronarnih arterija kod većine pacijenata. S obzirom da se ovom metodom direktno prikazuje i stijenka krvnih žila, CT je nakon intravaskularnog ultrazvuka (IVUS) najosjetljivija metoda za prikaz aterosklerotskog plaka. Značajno je osjetljivija od invazivne koronarografije koja prikazuje samo prohodan lumen krvne žile.

Indications for CCTA

Indications for CCTA^{9,10}:

- Chest pain with patients with intermediary risk
- An inconclusive stress test
- Coronary artery anomalies
- Cardiomyopathy evaluation
- Pre-operative workup with non-coronary cardiac operations

• Suspect aorta and pulmonary artery pathology

• Prior and following electrophysiologic procedures.

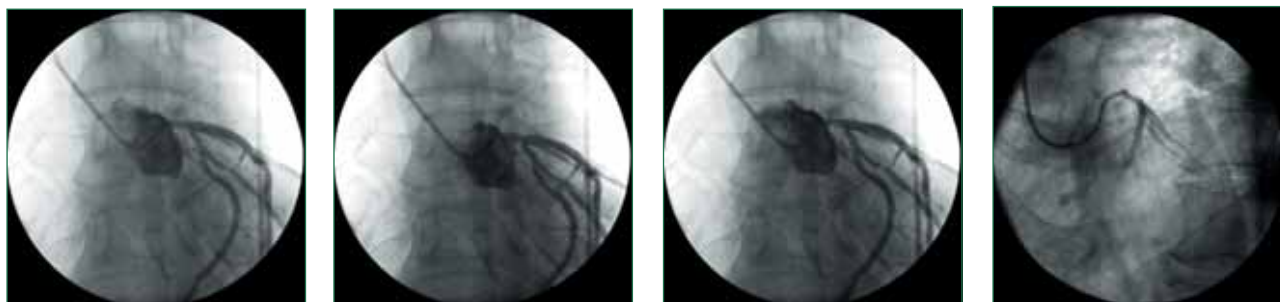
The most recent indications are related with 64-slice CT:

• Evaluation of chest pain and dyspnoea with patients with previous aortocoronary bypass or stent implantation

• Evaluation of acute chest pain in emergency.

The basic role of CCTA due to its negative predictive value is the exclusion of significant coronary heart disease with symptomatic patients with low or middle risk. The patients with typical clinical manifestations and high risk for coronary disease with clearly positive stress test have indication for invasive coronary angiography. The use of CCTA with asymptomatic patients is not recommended.

The modern devices have temporal resolution of ≤ 150 msec which with submillimeter spatial resolution provides a true presentation of coronary arteries in a great number of patients. Since the wall of blood vessels is directly shown by applying this method, CT is after intravascular ultrasound (IVUS) the second most sensitive method for presenting atherosclerotic plaque. It is much more sensitive than the invasive coronary angiography which only shows the passable lumen of the blood vessel.



The images of invasive coronary angiographies with nonsignificant stenosis of left main coronary artery.



The MSCT coronary angiography images after the invasive diagnostics and eight months later: reduction of the volume of mixed plaque in left main coronary artery with much higher density of plaque 8 months later (70HU vs. 35 HU) which indicates stabilization of the plaque by applying pharmacological therapy.



Uz navedeno CT omogućava analizu građe plaka, budući da može razlikovati masni sadržaj od kalcija pa čak i veziva. Novija istraživanja pokazuju da je, posebno kod većih krvnih žila, moguće pouzdano razlikovati plak koji je zbog "mekoće" svog sadržaja nestabilan^{14, 16}.

Prema najnovijim studijama 64-slojni CT ima vrlo dobru korelaciju s IVUS u evaluaciji aterosklerotskog plaka pa se postavlja pitanje da li je IVUS još zaista "zlatni standard" za evaluaciju aterosklerotskog plaka?

Glavno ograničenje ove metode je bila razmjerno visoka doza zračenja. Razvojem tehnologije ovdje su učinjeni značajni pomaci te se danas ne preporučuje izvoditi MSCT koronarografiju na uređajima s manje od 64 sloja. Ovo je dovelo i do bitnog proširenja indikacija, kao što su oslikavanje koronarnih stentova i prenosnica, čije oslikavanje na starijim generacijama MSCT nije bilo zadovoljavajuće¹¹.

Starija istraživanja doze zračenja kod CT koronarografije davala su vrlo šarolike rezultate, često s neprihvatljivo visokim dozama zračenja (do 30 mSv ekspozicijske doze). Ovakvi rezultati bili su posljedica korištenja neprimjerene tehnologije (uređaji s 4, 6 ili 16 slojeva) te nedovoljne vještine u pripremi i oslikavanju pacijenata.

Obzirom da doza zračenja kod MSCT uvelike ovisi o pripremi pacijenta i parametrima snimanja, ovo iziskuje posebno educirani kardiološko-radiološki tim i individual-

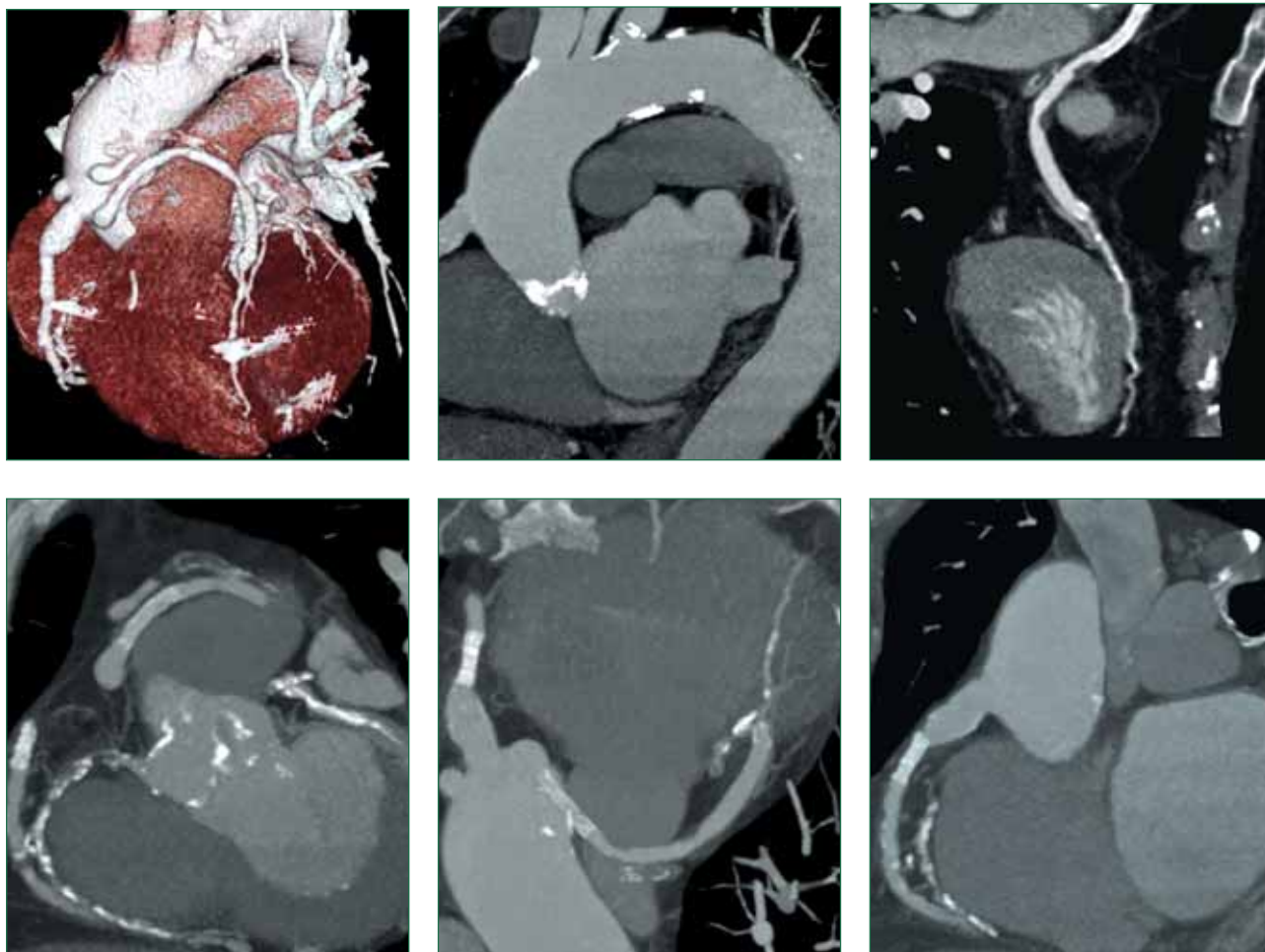
Besides the above mentioned, CT enables an analysis of the plaque composition since it may differentiate between fat contents and calcium and connective tissue as well. The recent researches show that especially in larger blood vessels it is with reliability possible to differ plaque that is due to its "softness" of its contents instable^{14, 16}.

According to the most recent studies 64-slice CT has a very good correlation with IVUS in evaluation of atherosclerotic plaque, so the issue is raised whether IVUS is still a "golden standard" for the evaluation of atherosclerotic plaque?

The main limitation of this method was proportionally high radiation dose. The development of the technology has resulted in significant improvements, consequently today CCTA is not recommended to be done on devices having fewer than 64 slices. This has led to significant widening of the indications such as imaging of coronary stents and bypasses whose imaging on older multislice CT generations was not satisfactory¹¹.

Subsequent researches of radiation dose during CT coronarography provided very different results, often with unacceptable high radiation dose (maximum 30 mSv exposition dose). Such results were the consequence of using inappropriate technology (devices with 4, 6 or 16 slices) and insufficient skill in preparing and imaging patients.

Since the radiation dose in CCTA greatly depends on the preparation of a patient and imaging parameters, this requires especially educated cardiac-radiologic team and



The condition following the quaternary aortocoronary bypass, two vein bypasses occluded, while the bypasses for the LAD and RCA as well as the stents in them are passable.



ni pristup svakom pacijentu, kako bi se uz čim manju dozu zračenja dobile snimke odgovarajuće dijagnostičke kvalitete.

Novija istraživanja na 64-slojnim uređajima i uz korištenje strategija za snižavanje doze zračenja, poput vjerojatno najrelevantnije PROTECT-I studije, pokazuju značajno manje doze zračenja^{6, 15, 17}. Na ovoj generaciji uređaja, uz njihovo primjereno korištenje, ekspozicijske doze zapravo su usporedive s onima kod invazivne koronarografije. Primjerice prosječna ekspozicijska doza kod CT koronarografije je izmjerena na oko 9 mSv, a kod invazivne koronarografije na oko 7 mSv. S obzirom na nepouzdanost mjerenja te metodologiju izračuna ekspozicijske doze, prema preporukama *International Commission on Radiation Protection* razlike u efektivnoj dozi do faktora 2 se zapravo ne smatraju značajnima^{6, 17, 18}.

Također je bitno napomenuti da se kod CT koronarografije zrači isključivo pacijent, dok je kod invazivne obrade zračenju izložen cijeli dijagnostički tim.

U PROTECT-I studiji je korištena generacija uređaja iz 2005. godine¹⁷. Odonda je CT tehnologija značajno napredovala te današnji uređaji postižu doze od 2-3 mSv kod većine pacijenata, a optimalne pacijente mogu se oslikavati i s dozama ispod 1 mSv¹⁹. Ovdje nažalost još ne postoji nezavisnih studija o dozi zračenja, no nekoliko takvih je u tijeku.

U **Tablici 1** su prikazane efektivne doze zračenja kod različitih metoda oslikavanja koje je na temelju najrecentnijih istraživanja sastavilo posebno tijelo *American Heart Association*⁶.

Examination	Effective Dose (mSv)	Range of Effective Dose (mSv)
Chest x-ray posteroanterior and lateral	0.1	0.05-0.24
CT abdominal (1 phase)	8	4-25
64-Slice coronary CTA* With tube current modulation	9	8-18
Dual-source coronary CTA* With tube current modulation	13	6-17
Prospectively triggered coronary CTA	3	2-4
Diagnostic invasive coronary angiogram	7	2-16
Thalium stress/rest	41	

Table 1. Representative values and ranges of effective dose estimates reported in the literature for selected radiological studies.

CTA = CT angiography

*CT studies published since 2005 only

Adapted from reference 6.

Ograničenja MSCT koronarografije

MSCT koronarografija ima i svoja ograničenja. Velika količina kalcija na koronarnim arterijama ometa evaluaciju prohodnosti koronarne arterije te je kod pacijenta s izrazitim kalcifikatima nemoguće procijeniti stupanj eventualne stenozе²⁰. Evaluacija luminalne stenozе otežana je kod pacijenta koji imaju ubranu frekvenciju srca, fibrilaciju atrijske ili učestalu ekstrasistoliju.

Respiratorni artefakt je moguć ukoliko pacijent nije suradljiv te ne prati upute o zadržavanju daha tijekom oslikavanja ili to ne može učiniti. Potrebno je naglasiti da izrazito pretili pacijenti, čiji je BMI preko 30, nisu optimalni kandidati za MSCT koronarografiju. Moguća je alergijska reakcija na kontrastno sredstvo.

individual approach to every patient as to obtain radiograms of adequate diagnostic quality with the smallest possible radiation.

Recent researches on 64-slice devices thereby using strategies for reduction of the radiation dose such as probably the most relevant PROTECT-I study show considerably smaller radiation dose^{6, 15, 17}. The exposition doses are actually on this device generation thereby using them adequately comparable with those used in invasive coronarography. For example, an average exposition dose in CT coronarography is measured at 9 mSv, and in non-invasive coronarography at around 7 mSv. Considering lack of reliability of measurements and methods of calculation of exposition dose according to recommendations of *International Commission on Radiation Protection* the differences in effective dose to factor 2 are actually not considered important^{6, 17, 18}.

It is worth mentioning that only a patient is radiated in case of CT coronarography, while the whole diagnostic team is exposed to radiation in case of invasive diagnostics.

In PROTECT-I study the device generation from 2005 was used¹⁷. Since then, CT technology has been greatly improved and today's devices reach doses of 2-3 mSv in most of the patients, while optimum patients may be imaged with the doses below 1 mSv¹⁹. Here, unfortunately there are no non-independent studies of radiation doses, but several studies of that type are underway.

In **Table 1** effective radiation doses are presented when using different imaging methods prepared according to the most recent researches by a special body *American Heart Association*⁶.

Limitations of CCTA

MSCT coronarography has its limits. The great quantity of calcium in coronary arteries obstructs evaluation of passage of coronary artery, and with patients with very high calcifications it is impossible to evaluate a degree of potential stenosis²⁰. The evaluation of luminal stenosis is made difficult with patients having accelerated heart frequency, atrial fibrillation or frequent premature beats.

Respiratory artifact is possible if a patient is not cooperative and does not follow instructions for keeping breath during imaging or if he/she cannot do it. It is worth mentioning that very obese patients whose BMI is over 30 are not good candidates for CCTA. Allergic reaction to contrast agent is possible.



Zaključak

Sve više se postavlja pitanje je li je MSCT koronarografija spremna zamijeniti dijagnostičku invazivnu koronarografiju, a neki se čak pitaju: je li došao kraj invazivnoj koronarografiji kao dijagnostičkoj metodi?^{21, 22}

S tim u vezi mogli bi zaključiti da invazivna koronarografija u kombinaciji s izrazito pozitivnim stres testom ostaje metoda izbora kod pacijenata s visokom vjerojatnošću KBS i očekivanom koronarnom intervencijom (PCI). Međutim, kod većine pacijenata s malim ili srednjim rizikom KBS metoda MSCT koronarografije može biti pouzdana, klinički učinkovita i ekonomski isplativa neinvazivna alternativa invazivnoj koronarografiji.

Received: 23rd Jun 2010 Updated 8th Jul 2010

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