Original Research Paper

Volume-9 | Issue-2 | February-2019 | PRINT ISSN - 2249-555X

Medical Science

DETERMINATION OF MASS DENSITY OF ATHEROSCLEROTIC NON-CALCIFIED PLAQUE

Susama Rani Mandal	Government Medical College, Kannauj, Uttar Pradesh, 209725, India
Avinav Bharati	Dr RML Institute of Medical Sciences, Lucknow, Uttar Pradesh, 226010, India
Pratik Kumar*	Medical Physics Unit, Dr B.R. Ambedkar IRCH, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, 110 029, India *Corresponding Author

ABSTRACT **Aim:** In a previous study Dual Energy CT is employed to determining effective atomic number and electron density of atherosclerotic coronary artery plaque which is based on the measurement of linear attenuation coefficient of the atherosclerotic coronary artery plaque at two different energies. This study explores the way to measure the electron density of tiny and porous coronary plaque and verifies the Dual Energy CT - non invasive method of determination of electron density.

Density of plaque so obtained by Dual Energy CT was verified, by pycnometry method which was utilized to independently measure the actual density of plaques. The reliability of pycnometry method was also further standardized.

This study, being first of its kind reports the actual density of coronary artery plaque and the results clearly show the consistency between Dual Energy CT results and of pycnometry measurement. This indicates that electron density as obtained by Dual Energy CT can be used to characterize the plaque and proves the reliability of the method applied for calculating ρe and Zeff from Dual Energy CT data, it can be applied to gather vast information for clinical purpose.

KEYWORDS : Dual Energy Computer Tomography; Effective electron density ; coronary artery plaque; Pycnometry

1. INTRODUCTION

Dual Energy Computed Tomography (DECT) images are the distribution of x-ray attenuation data of scanned organ or object with respect to x-ray attenuation in water which is called Hounsfield Unit (HU). It is obvious that HU values of the CT images would depend upon those physical and chemical properties of the scanned material which affects x-ray attenuation. These are Atomic number (Z_{eff}) (Effective Atomic number in case of compound or mixture) and Electron density (ρ_e)[1-5]. As reported in previous study[6] these parameters can be used to determine the vulnerable and stable coronary artery atherosclerotic plaque this is important as non-invasive characterization by DECT scan may help in planning strategy or control of disease.

Next task is to verify DECT outcomes by an independent method, that is, to verify the effective atomic number (Z_{eff}) and the electron density (ρ_e) of coronary artery plaque as obtained non-invasively by DECT. Scanning Electron Microscope-Energy Dispersive X-ray Spectroscopy (SEM-EDS) (ref) verifies Z_{eff} obtained by DECT. In this study the ρ_e of artery plaques obtained non-invasively by DECT is compared with the actual density of plaques measured physically for its accuracy and reliability. Physical measurements complicated due to porous nature of plaques and limited by very small quantity that could be extracted for measurement. This study elaborated how pycnometry is found to be the best suitable method for physical measurement and this pycnometry method is also verified by another method called Density Gradient method and hence confirmed the standard. Our extensive search of literature revealed that there was no study reporting the attempts to measure the mass density of the atherosclerotic coronary plaque. This method can confidently be used as a cheaper alternative to commercial phantom based procedure to determine electron density in radiotherapy[7-11].

2. MATERIALS AND METHODS

DECT scan of excised coronary artery from cadaver heart is carried as per protocol reported earlier[6] and Maximum Intensity Projection (MIP) mode was used to evaluate the presence of non-calcified plaque in the Left anterior descending artery (LAD) and the distance between coronary ostium to the plaque was measured. In total, 32 plaque samples were accessed by DECT and from each of these 32 samples representative sections were submitted for histopathological and SEM-EDS analysis. From these samples small quantity of plaque was manually extracted for physical measurement of mass density. HU data of plaque at 100 and 140 kVp were read and used to obtain effective atomic number (Z_{eff}) and electron density (ρ_e) for all samples[6].

2.1 Sample preparation

Since size and length of the plaque varies from sample to sample thus not all samples were sufficient enough in terms of quantity to be included for density measurement, in total only19 samples were found to be sufficient enough to be extracted manually to carried out physical measurement of mass density. Five of these plaque samples were taken for density measurement by buoyancy method described below and four in density measurement by gradient column also described below, remaining 11 samples were used up for density measurement by pycnometry.

2.2 Density measurement of real plaque

I. Buoyancy method

Archimedes' principle was used to measure the mass density of the plaque. For this purpose, five different atherosclerotic coronary artery plaques were dissected, and kept in 10% formalin for at least 1 week, and were then dried. At first, weight of the dried soft plaque were measured thereafter, plaques were put in distilled water kept in a graduated thin capillary tube. After putting in water, these dry materials were seen to float but they sank after sometime as the pores got filled with sufficient amount of water. Once the sample sank completely, the rise in the level of water in the thin tube was measured. The level of water in capillary tube was measured by a traveling microscope. Thus the instruments chosen were of sufficient accuracy. However, the results were not reproducible and this method was abandon.

2.3 Density gradient column

For this purpose, four different soft plaques samples were used. A density gradient column is a column of liquid that varies in density with height. A sample is placed in the liquid and is observed to determine at what vertical level in the column the sample is suspended. The density of the liquid at that level is the density of the sample, and that value is determined by standard known density of the liquid. Density gradient column was designed by us by suitably selecting the liquids, a preliminary idea of their densities were obtained from available literature[12-17]. Density of all the liquids used in density gradient column were independently determined using commercially available specific gravity bottle and their values were: Liquid paraffin=0.86322 g/cm^3, Mustard oil = 0.91002 g/cm^3, Milk = 1.031022 g/cm^3, Glycerine = 1.233 g/cm^3, Honey = 1.422 g/cm^3, Sugar syrup = 1.501 g/cm^3, thus a column with density ranging from 0.863 g/cm^3 to 1.501 g/cm^3. The whole arrangement of density gradient is shown in Fig 2. However, the plaque or tissue absorbs the immersion liquid and then result could no longer be taken to be valid. Thus this method couldn't give reproducible results in case of plaque material as such substances were highly porous and absorbed the liquid when they were immersed in. However, this method gives accurate values for non-porous materials as described in Table II. This method gave gross results (in terms of magnitude) which were further refined by pycnometer described below.

2.4 Pycnometer method with different immersion liquids to measure mass density of coronary artery plaque

In pycnomtry method four weighings were performed,

W_1 = Weight of empty pycnometer,

W_2 = Weight of pycnometer + specimen,

W_3 = Weight of pycnometer + specimen + liquid

W_4 = Weight of pycnometer filled with liquid.

The density of the specimen is then given by:-

Density of specimen= [density of immersion liquid]×[$(W_2-W_1)/((W_4-W_1)-(W_3-W_2))$] (1)

In pycnometry specific gravity bottle of 4.1 ml as shown in fig 1 was used with different immersion liquids honey and glycerine and mercury. Figure 1 shows experimental setup with pycnometer. Table I gives comparative results of pycnometry with different type of immersion liquid.

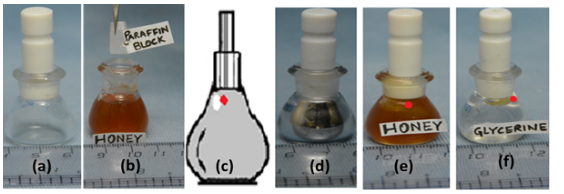

Figure1. (a) A Customized specific gravity bottle of 4.1ml , (b) showing experimental set up with different honey as immersion liquid. (c). schematic diagram depicting sample (pointed by a red dot) suspended or floating in the immersion liquid contained in pycnometery. Fig (d), (e), and (f) shows real pycnometer with mercury, honey and glycerine respectively.

Table I. Result of Density in pycnometer using honey, glycerine and mercury as immersion liquid.

Substance	Density in pycnometer using honey	Density in pycnometer using glycerine	Density in pycnometer using mercury ± Standard deviation	Expected mass density from literature (g/cc)	References
Cheese	0.917674	1.052852	1.1486 ±0.032665	0.384-1.15	19
Bee wax	1.039933	0.988837	0.9486 ±0.049481	0.95-0.97	20
Paraffin	0.941425	0.917736	0.8745 ±0.038308	0.9	21/vendor specified
Sucrose	1.620329	0.722008	1.5092 ±0.049609	1.5	-
Alum	2.25695	2.01065	1.5052771 ±0.035397	1.5	vendor specified
PMMA	2.000968	1.755135	1.141021 ±0.028777	1.15-1.19	22
Aluminum block	2.159569	1.89251	2.643966 ±0.107617	2.699	23
Chicken Fat	0.826608	0.862223	0.9583 ±0.049289	0.88-0.89 (viscous liquid)	24, 25
Chicken Meat or Flesh	1.052602	0.961245	1.112145 ±0.026493	1.121	19

2.5 Pycnometer with mercury as immersion liquid- Successful attempt

Lastly, attempt was performed with immersion liquid as mercury (mass density of 13.6 g/cc).

Lastly, attempt was performed with immersion liquid as mercury (mass density of 13.6 g/cc). For optimizing and standardizing pycnometer for measuring the mass density of soft plaque calibration substance as mentioned in table II were chosen due to the fact that their densities could be found by other means as well, (that is, by density gradient column method) so as to verify the reproducibility and reliability of pycnometry. Table I reports results with pycnometry with immersion liquid as honey, glycerine and mercury for different calibration material such as Aluminum block and Polymethyl methacrylate (PMMA) pieces and other substance such as cheese, beewax, paraffin wax, sucrose, alum, chicken fat and meat or flesh as these substances (fat and waxes) were similar to plaque composition since plaque mainly contains fiber and lipid. From literature their expected mass density or range of mass density were found and is summaried in Table II. Few of these materials were obtained from M\S Merck Chemicals, hence their densities were vendor specific. In Figure 1(c) gives the schematic diagram of pycnometer with sample floating at the top indicated by a marker. Figure 1(d), 1(e), and 1(f) showed the pycnometer with mercury, honey and glycerine inside respectively. Figure 1(d) shows that sample will always be floating in the liquid as mercury is denser than the sample whereas with honey and glycerine this might not true be always. With mercury as immersion liquid in pycnometer the results are tabulated in table I.

3. RESULTS

3.1 Result of Density measurement by pycnometer

The mass density of plaque were calculated from electron density (ρ_e) (ρ_e obtained non-invasively from DECT) [4-6] and the mass density so found is referred as $\rho_{(calculated)}$.

Z_{eff} and ρ_e from DECT were non-invasively. Further mass density from ρ_e, that is, $\rho_{(calculated)}$ is calculayted using following equation[15,16]

$$\rho_{(calculated)} = -0.1746 + (1.176 * \rho_e/\rho_{ewater}) \qquad (2)$$

where $\rho_e/\rho_{e\,water}$ is called the relative electron density of plaque with respect to electron density of water. Mean ρ_e and $\rho_{(calculated)}$ values are tabulated in table III.

The mass density by pycnometry with mercury as immersion liquid is referred as $\rho_{(actual)}$. Table I reports results with pycnometry with immersion liquid as honey, glycerine and mercury for different calibration materials At first density measurements in pycnometry with performed by honey and glycerine. Main drawback of these immersion liquids was that plaque samples would absorb the immersion liquid leading to non-reproducible results thus were rejected. The results by mercury pycnometer is the averaged result of three consecutive density measurements.

3.1 Testing of the reliability pycnometry method by Density Gradient Method

Reliability of the pycnometry method was checked by comparing the results got by this method with those from the liquid density gradient column. However, the later method (Density gradient) gives us gross value (in term of magnitude) for non-absorbing material and proves that the results obtained from pycnometry were close to actual values. Density Gradient method is reliable for substances such as cheese, beewax, paraffin, sucrose, Alum , PMMA and Aluminium block which do not dissolve or absorb the liquids in which they are held up during the time (10-15mins) of experiment. In certain cases where the material was seen to be immersed partially in two different liquid (in other words it was held at the interface of two liquids) a finer study was done by carefully mixing the two liquids of the interface in proper proportion and thus obtaining a finer control over the density gradient. For example, from density gradient column we observed that paraffin block got suspended at the interface of mustard oil and liquid paraffin as shown in figure 2.

In order to calculate exact density value of that level in the density gradient column we prepared a solution mixing mustard oil and liquid paraffin in different ratios from 1:1 to 9:1 respectively and we found that Paraffin block got suspended in 8:1 mixture of mustard oil with liquid paraffin. Similarly, Cheese got suspended in 1:1 solution of glycerin with milk. Therefore, we measured exact density of milk and glycerin (1:1) solution and solution of mustard oil with liquid paraffin (8:1) by commercially available specific gravity bottle. From density gradient column mass density of bee wax was obtained to be more than 0.91002 as it sank in mustard oil but floated in milk in the density gradient column. For Aluminium block and PMMA pieces we used the Archimedes kit to obtain their density 2.699 and 1.151g/cc respectively which matches with the density obtained in pycnometry experiment using mercury. Table II summarizes the mass density obtained from Pycnometry and density gradient column. Results proved the consistency and reliability of pycnometry method when immersion liquid was mercury and thus it could be applied for plaque samples.

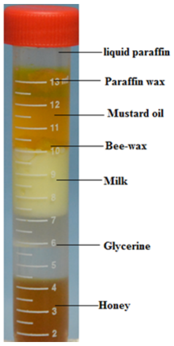

Figure 2: Density gradient column arrangement showing different layers of liquid with paraffin wax block floating at the interface of liquid paraffin and mustard oil and bee-wax settled at the bottom of mustard oil.

Table II. Comparing the result by Pycnometry and Density gradient method

Substance	Density in pycnometer using mercury	Density by density gradient
Cheese	1.1486	1.13522
Bee wax	0.9486	>0.91002
Paraffin	0.8745	0.9048193
Sucrose	1.5092	1.501 (got suspended in sugar syrup)
Alum	1.5052771	1.501 (got suspended in sugar syrup)

Densities of liquids used in density gradient column: Liquid paraffin=0.86322 g/cm3, Liquid paraffin + Mustard oil (8:1)=0.9048193g/cm3 , Mustard oil=0.91002 g/cm3, Milk=1.031022 g/cm3,Milk+ Glycerin(1:1)=1.13522 g/cm3 , Glycerin=1.233 g/cm3, Honey=1.422 g/cm3, Sugar syrup=1.501 g/cm3

3.3 Density measurement of plaque samples using pycnometer

Once reliability and consistency of pycnometry method for finding the plaque's density was established we proceeded with finding the mass density of plaque by pycnometry method as stated in section –only 11samples were taken to measure the mass density by pycnometry and results of the measurement is summarized in Table III

Table III. Density of plaque specimen by DECT ($\rho_{calculated}$) and by pycnometry method (ρ_{actaul})

Serial no.	Eldectron Density by DECT (ρ_e)	Density by DECT $\rho_{(calculated)}$	Density by Pycnometry $\rho_{(actual)}$	$\rho_{(calculated)}$ / $\rho_{(actual)}$
1	3.513407	1.07745	1.049	1.027122
2	3.556552	1.092826	1.045	1.045766
3	3.586478	1.10349	1.101	1.002262
4	3.442617	1.052224	1.076	0.977903
5	3.484417	1.06712	1.05	1.016304
6	3.500696	1.072921	1.061	1.011235
7	3.492814	1.070112	1.07	1.000105
8	3.571579	1.098181	1.047	1.048883
9	3.446421	1.053579	1.112	0.947463
10	3.418897	1.043771	1.054	0.990295
11	3.487261	1.068133	1.075	0.993612
12	3.432007	1.048442	1.0513	0.997282
13	3.467659	1.061148	1.645	0.645075
14	3.639311	1.122318	1.125	0.997616
15	3.551556	1.091045	0.866	1.259868
16	3.541618	1.054487	0.878	1.201011
17	3.40587	1.042509	1.045	0.997616
18	3.472054	1.025653	1.05	0.976812
19	3.56702	1.0938	0.991	1.103733

After comparing ρ(calculated) with ρ(actual results for the density obtained by DECT to density obtained by pycnometry were close to unity. That is the mean value of ρ(calculated) / ρ(actual) ="S" is 1.01314 ± 0.01992. Considering the error to be normally distributed we conclude with 99% confidence that ratio " S " lies between the acceptable range [0.994, 1.032] with maximum error of 0.154%.

4. DISCUSSION

Methods, though based on sound principle, could not give reproducible results due to porosity of the plaque samples such as Buoyancy method and density gradient. Next attempt was made with pycnometry. The Pycnometer method is used, in general, for determination of the specific gravity of solid particles of both fine grained and coarse grained soils8. The thorough review of literature revealed that Muccigrosso et al[17] have found density of alumina particles (0.01cm3) using pycnometry which is based on the principle that the mass of the specimen is determined by weighing, and its volume is obtained by weighing the liquid displaced from the pycnometer by the specimen. Customized specific gravity bottle of 4.1 ml shown in Fig 1 was used, since commercial pycnometer or specific gravity bottle less than 10 ml was not available. Such a small volume specific gravity bottle was needed because of extremely small size of plaque content in arteries. One essential condition was that immersion liquid must be dense for obtaining greater precision, like honey, glycerol and finally mercury. First attempt was performed with honey (1.422 g/cc) but adherence of air bubble (shown by arrow head in Figure 1) to the surface of the immersed specimen (plaque) caused an artificial increase in volume and buoyancy. Thereafter, second attempt was made by replacing the immersion liquid with glycerol (1.233 g/cc). This time adherence of air bubble to the surface of the immersed specimen was much reduced but as density of glycerol is less than that of honey, immersed specimen absorbed glycerol leading to no improvement in the results. Moreover, repeated experiments showed that results with honey and glycerol were not reproducible though results using honey and glycerine were near the values reported in literature[12-15] for few substances. In case of mercury the question of air bubble didn't arise. Air bubbles were too light to be trapped in mercury and they were pushed up due to buoyancy to escape through the capillary in pycnometer stopper. Results were reproducible and were close to the values found in literature for various material used in these experiments. Table I reports the results obtained by pycnometry using honey, glycerol and mercury respectively. With mercury reproducible results were obtained thus mercury is chosen as immersion liquid which made this method applicable for plaque density measurements. Further standardizing the pycnometer as a density measurement tool required checking its reliability by an independent method and that method was chosen to be density gradient method. As tabulated in table II which proves its reliability. In table III reports the mass density of plaque as measured by pycnometer. The density of soft plaque obtained by DECT appears to be in good agreement with density measured by pycnometer with maximum error less than 1% and thus it confirms that electron density predicted by the inversion algorithm is reliable and accurate. In other words, the pycnometry proved that the DECT could be used to determined ρ_{eff} of the artherosclerotic coronary artery plaque.

Also, conversion of CT number or HU values to electron density is a crucial process which in turn determine patient dose calculation accuracy[7-11]. These commercial phantom based studies have been employed to grossly determine electron density of lung, soft tissue, bone, air water, etc. However, areas where precise differentiation in electron density is require like prosthetic , implants, renal stones and plaque as their presence affect dose distribution in surrounding in such, a scenario pycnometry is the answer. Pycnometry is much more economical way than commercial phantom based method to check or determine electron density. In present study puycnometry emerges out to be the best suitable method to check as well as determine electron density thus proves the reliability of DECT[6] method to determine electron density.

5. CONCLUSION

The measurement of the density of the human plaque has not been reported earlier and the reliable measurement becomes difficult due to porosity of the plaque and also due to its tiny quantity. We conclude that the best suitable method for determining the density of the plaque was pycnometry with mercury as immersion liquid because surface tension effect wouldn't allow mercury to enter porous material such as plaque thus overcoming the problem due to adherence of air bubble to the surface of the immersed specimen which caused an artificial increase in volume and buoyancy. Once we know the density of plaque it could be compared with the density obtained by DECT. This study reveals that the ratio of the density obtained by pycnometry and the density derived by DECT to be close to unity with 99% confidence which means maximum error of 0.154%. It was considered acceptable and implied that the result of density measurement was reliable and satisfactory.

ACKNOWLEDGMENT

Author would like to thank Indian Council of Medical Research (ICMR) for financing the project. Dr R.R. Haghighi and Dr Suresh Perumal is thanked for their valuable inputs. The author thanks Mrs. Meenakshi Sharma for her constant help in Lab.

REFERENCES

1. http://www.ncbi.nlm.nih.gov/pubmed/?term=Landry%20G%5BAuthor%5D&cauthor=true&cauthor_uid=24025623" Landry G, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Seco%20J%5BAuthor%5D&cauthor=true&cauthor_uid=24025623" Seco J, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Gaudreault%20M%5B Author 5D&cauthor=true&cauthor_uid=24025623"Gaudreault M, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Verhaegen%20F%5BAuthor%5D&cauthor=true&cauthor_uid=24025623" Verhaegen F., Deriving effective atomic numbers from DECT based on a parameterization of the ratio of high and low linear attenuation coefficients., Phys. Med. Biol. 58 ,6851–6866, (2013) doi: 10.1088/0031-9155/58/19/6851
2. "http://www.ncbi.nlm.nih.gov/pubmed/?term=Bourque%20AE%5BAuthor%5D&cauthor=true&cauthor_uid=24694786" Bourque AE, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Carrier%20JF%5BAuthor%5D&cauthor=true&cauthor_uid=24694786" Carrier JF, "http://www.ncbi.nlm.nih.gov/ pubmed/?term=Bouchard%20H%5BAuthor%5D&cauthor=true&cauthor_uid=24694786" Bouchard H, A stoichiometric calibration method for dual energy computed tomography", Phys. Med. Biol. 59 , 2059–2088,2014. doi: 10.1088/0031-9155/59/8/2059
3. "http://www.ncbi.nlm.nih.gov/pubmed/?term=Haghighi%20RR%5BAuthor%5D&cauthor=true&cauthor_uid=21992344" Haghighi RR1, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Chatterjee%20S%5BAuthor%5D&cauthor=true&cauthor_uid=21992344" Chatterjee S, "http://www.ncbi.nlm.nih.gov/ pubmed/?term=Vyas%20A%5BAuthor%5 D&cauthor=true&cauthor_uid=21992344" Vyas A, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Kumar%20P%5BAuthor%5D&cauthor=true&cauthor_uid=21992344" Kumar P, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Thulkar%20S%5BAuthor%5D&cauthor=true&cauthor_uid=21992344" Thulkar S, X-ray Attenuation Coefficient of Mixtures: Inputs for Dual-Energy CT, Med. Phys. 38(10), 5270-5279 (2011). doi: 10.1118/1.3626572
4. Landry G, Granton PV, Reniers B, et al. (2011) Simulation study on potential accuracy gains from dual energy CT tissue segmentation for low-energy brachytherapy Monte Carlo dose calculations. Phys. Med. Biol. 56(19):6257.
5. Haghighi R R, Chatterjee S, Tabin M, et al. DECT evaluation of non-calcified coronary artery plaque. Med. Phys. 42, 5945 (2015); http://dx.doi.org/10.1118/1.4929935 Mandal SR, Bharati Avinav, Haghighib RR et al. (2018) Non-invasive characterization of coronary artery atherosclerotic plaque using dual energy CT: Explanation in ex-vivo samples. Phys. Medica. 45: 52–58.
6. Ramos Garcia I, Pérez Azorin J.F, Almansa J.F. et al.(2016). A new method to measure electron density and effective atomic number using dual-energy CT images, Phys. Med. Biol. 61(1): 265-279.
7. Saito M and Sagara S. (2017). A simple formulation for deriving effective atomic numbers via electron density calibration from dual-energy CT data in the human body, Med. Phys. 44(6): 2293-2303.
8. Lalonde A, Bär E, and Bouchard H.(2017). A Bayesian approach to solve proton stopping powers from noisy multi-energy CT data, Med. Phys. 1-10.
9. Sakata D, Haga A, Kida S, Imae T et al. (2017) Effective atomic number estimation using kV-MV dual-energy source in LINAC, Phys. Medica. 39: 9-15.
10. Bourque A. E, Carrier J. F, and Bouchard H. (2014). A stoichiometric calibration method for dual energy computed tomography. Phys. Med. Biol. 59(8): 2059-2088.
11. "http://www.ncbi.nlm.nih.gov/pubmed/?term=Becker%20CR%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Becker CR, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Nikolaou%20K%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Nikolaou K, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Muders%20M%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Muders M, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Babaryka%20G%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Babaryka G, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Crispin%20A%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Crispin A, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Schoepf%20UJ%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Schoepf UJ, "http://www.ncbi. nlm.nih.gov/pubmed/?term=Loehrs%20U%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Loehrs U, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Reiser%20MF%5BAuthor%5D&cauthor=true&cauthor_uid=12692681" Reiser MF, Ex vivo atherosclerotic plaque characterization with multi-detector-row CT, Eur Radiol, 13, 2094-2098 (2003).
12. "http://www.ncbi.nlm.nih.gov/pubmed/?term=Maurovich-Horvat%20P%5BAuthor%5 D&cauthor=true&cauthor_uid=23012461" Maurovich-Horvat P, "http://www.ncbi. nlm.nih.gov/pubmed/?term=Schlett%20CL%5BAuthor%5D&cauthor=true&cauthor_uid=23012461" Schlett CL, "http://www. ncbi.nlm.nih.gov/pubmed/?term =Alkadhi%20H%5BAuthor%5D&cauthor= true&cauthor_uid=23012461" Alkadhi H, "http://www.ncbi.nlm.nih.gov/pubmed/?term=Nakano%20M%5BAuthor%5D&cauthor=true&cauthor_uid=230