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REVIEW

Imaging

Cardiac imaging: does radiation matter?

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The use of ionizing radiation in cardiovascular imaging has generated considerable discussion. Radiation should not be considered in isolation, but rather in the context of a careful examination of the benefits, risks, and costs of cardiovascular imaging. Such consideration requires an understanding of some fundamental aspects of the biology, physics, epidemiology, and terminology germane to radiation, as well as principles of radiological protection. This paper offers a concise, contemporary perspective on these areas by addressing pertinent questions relating to radiation and its application to cardiac imaging.

Keywords Cardiac imaging • Ionizing radiation

Recently, the potential risks associated with cardiovascular imaging have generated considerable discussion. This attention has been fuelled by the rapid increase in the use of imaging procedures worldwide as well as new imaging modalities such as cardiac computed tomography, which has further broadened the potential indications of non-invasive imaging tests. The number of CT scans of all types performed in the USA has quadrupled since 1993, and the same increasing trend has also been observed in Europe.[1] The increase in imaging utilization has led to a nearly six-fold increase in the per capita dose of radiation from medical imaging noted to have occurred in the USA between 1982 and 2007.[2] This has lead to worries about the potential harms arising from medical imaging using ionizing radiation, most notably cancers, and calls for more efficient radiation protection measures and, in its extreme, questioning the justification of imaging use in large populations. The discussion until now has rarely focused on the benefits of imaging tests, although for proper context the risks of a test should always be weighed against the risks if disease remains undetected, detected at a later stage, incorrectly prognosticated, or suboptimally treated.

An educated discussion of the benefits, risks, and costs of cardiovascular imaging is predicated on an understanding of both the specific benefits of each imaging modality as well as relevant aspects of radiation biology, physics, and epidemiology, and requires clear usage of the sometimes labyrinthine terminology used to describe radiation. In this paper, we address several fundamental questions related to radiation in cardiac imaging, aimed at providing a better understanding of why radiation matters and improving the discourse on the role of radiation in cardiac imaging.

What is radiation?

Radiation is the propagation or emission of energy in the form of particles or waves travelling through space. Electromagnetic radiation is a type of radiation in which there are self-propagating waves, and is further classified on the electromagnetic spectrum based on the wavelength, frequency, or energy of these waves, ranging from radio waves (highest wavelengths, lowest frequencies and energies) to gamma rays and X-rays (lowest wavelengths, highest frequencies and energies). The distinction between gamma and X-rays is that gamma rays are emitted by an atom's nucleus, whereas X-rays are emitted by electrons outside the nucleus.

Another classification of radiation is the distinction between ionizing and non-ionizing radiation. Ionizing radiation has enough energy to ionize atoms, e.g. to enable an electron to move out of its orbit, whereas non-ionizing radiation does not. Most types of electromagnetic radiation, such as visible light, are non-ionizing, but higher energy electromagnetic radiation such as gamma rays and X-rays is ionizing, as are several types of particulate radiation.

What are potential benefits and risks of radiation?

Ionizing radiation is applied to a patient in the context of medical imaging in order to reconstruct important anatomic or physiological information from data collected about the pattern of radiation observed on detectors near the patient. This information can be

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used in conjunction with prior information to provide a better understanding of the patient's diagnosis, prognosis, or treatment response, or to guide therapy.

However, by direct damage or via production of free radicals, this same ionizing radiation also has the ability to modify cells and their genetic material, thereby leading to potentially deleterious effects. Radiation's deleterious effects are typically classified into two types—*stochastic effects* which are due to radiation-induced mutations, and *deterministic effects*, otherwise known as tissue reactions, which are due to radiation-induced cell death. In cardiac imaging, the primary stochastic effect of concern is cancer, while the primary deterministic effect of concern is skin and/or hair changes.[3] Deterministic effects only occur above a threshold level of radiation, which is generally higher than levels occurring from a single non-invasive imaging procedure, so stochastic effects are the primary concern in cardiac imaging. However, deterministic effects can occur from invasive fluoroscopic procedures, and have been observed in rare cases in CT angiography/perfusion studies of the brain.[4]

In which imaging modalities is ionizing radiation used?

Of current imaging modalities, ionizing radiation in the form of X-rays is used in a variety of related modalities, which are given special names depending on their X-ray sources and detector configurations and position(s) used to reconstruct images; these include projection imaging with conventional X-ray (film detector), computed radiography (cassette with photostimulable storage phosphors), direct/digital radiography (solid-state detectors), and fluoroscopy (continuous beam with movable source and detector), as well as volumetric imaging with multidetector-row computed tomography (source and arrays of solid-state detectors mounted on rotating gantry) and electron-beam computed tomography (electromagnetically deflected beam of X-rays). Ionizing radiation is also used in nuclear medicine, where radiopharmaceuticals' decay processes are detected, localized, and quantified. Depending on the nature of the images reconstructed and the decay events detected, the imaging modality may be referred to as planar nuclear imaging, single-photon emission computed tomography (SPECT), or positron-emission tomography (PET). Other common imaging modalities, such as ultrasonography and magnetic resonance imaging, obtain images by taking advantage of other physical processes which do not require patients' exposures to ionizing radiation.

How is radiation measured in medical imaging?

There are a variety of approaches used to quantify the amount of ionizing radiation received by patients undergoing medical imaging procedures. It is typical to estimate some quantity reflecting the concentration of energy deposited in tissue by the radiation, and depending on the context this concentration and its units are given special names. *Absorbed dose* refers to the unweighted concentration of energy and is usually reported in units of Gray (Gy), a special term for Joules per kilogram. Absorbed dose is sometimes weighted by a radiation weighting factor to reflect the type of energy, since not all types of energy are associated with the same risk of stochastic effects such as cancer incidence. When this weighting factor, equal to 1 for X-rays and gamma rays, is applied, the concentration is referred to as *equivalent dose* and the special unit for Joules per kilogram is called the Sievert (Sv). In turn, equivalent dose is sometimes weighted by a second weighting factor, to reflect that the same concentration of energy has differing risks of stochastic effects depending on the tissue or organ receiving the radiation. When equivalent dose is weighted again by this tissue weighting factor, it is referred to as *weighted equivalent dose*, which also is measured in Sieverts. The most commonly used whole-body measure of radiation risk is the *effective dose*, defined as the sum of weighted equivalent doses over all organs in the body. Effective dose is by its definition determined for a gender-averaged, non-obese reference individual, rather than for a specific individual, and since tissue weighting factors were updated in 2007,[5] effective dose calculations have changed somewhat. Many scanners report a modality-specific measure of radiation exposure, such as dose-length product for CT or kerma-area product for fluoroscopy (Table 1). For some of these metrics, multiplication by a standard conversion factor or *k* factor can be used to estimate effective dose. Such conversion factors can be found in European Commission publications,[6,7] although recent work suggests that these conversion factors will in some cases underestimate effective dose of cardiac imaging procedures.[8–10]

Table 1 Common modality-specific dosimetry terminology

Projection radiography (X-ray, computed/digital/dental radiography)
Entrance surface dose/entrance surface air kerma
Dose-area product (DAP)/Kerma-area product (KAP)
Exposure index
Fluoroscopy
Fluoroscopy time
Fluoroscopy runs
Cine time
Cine runs
DAP/KAP
Cumulative dose/air kerma at the interventional reference point ($K_{a,r}$)
Peak skin dose
Computed tomography
CT dose index, weighted ($CTDI_w$)
CT dose index, volume ($CTDI_{vol}$)
Dose-length product (DLP)
Mammography
Incident entrance air kerma
Average glandular dose
Nuclear medicine
Administered activity (MBq)

How much radiation do our patients receive?

The amount of radiation received by patients from individual cardiac imaging procedures involving X-rays or nuclear medicine varies depending on both the modality as well as the specific protocol performed. For example, low-dose stress-only myocardial perfusion imaging with technetium-99 m, using standard EANM/ESC-recommended activity[11] of 450 MBq, has an effective dose of 3 mSv, but if rest imaging with a standard activity of 1350 MBq is performed on the same day then the effective dose is 13 mSv. In cardiac CT, helical scanning with retrospective selection of the phase of the cardiac cycle used for image interpretation is associated with high effective dose, typically on the order of 20 mSv, however use of scan modes that prospectively select and limit radiation exposure to this phase can be associated with doses 5 or 10 times lower. Radiation dose from percutaneous coronary intervention depends markedly on many factors including fluoroscopy and cine times and frame rates, magnification, beam collimation, and table height. Typical effective doses for some standard cardiac imaging procedures and other common exposures are summarized in Table 2.

It is important to note that the patients undergoing cardiac imaging may have undergone previous testing involving ionizing radiation exposure. In analyzing administrative claims data from between 2005 and 2007 in a cohort of nearly 1 million individuals covered by a single payer in USA, Chen *et al* observed that 9.5% of individuals underwent at least one cardiac imaging procedure involving ionizing radation. Of these patients, the median cumulative effective dose over 3 years was 16 mSv (range 1.5–544 mSv).[20] In one series of 1097 consecutive patients undergoing myocardial perfusion imaging at a single centre in the USA, patients undergoing myocardial perfusion imaging underwent a median of 15 procedures (inter-quartile range: 6–32) involving ionizing radiation, with a median cumulative effective dose estimated at 64 mSv (inter-quartile range: 35–123 mSv; range 7–918 mSv), over a 20 year period.[21] In another series of 50 consecutive patients admitted to a cardiology service in Italy, a median of 36 radiation procedures were noted (inter-quartile range: 23–46), with a median cumulative effective dose of 61 mSv (inter-quartile range: 36–101 mSv; range 3–441 mSv) over a 26-year period.[20,22]

Table 2 Typical effective doses

Source	Typical effective dose (mSv)
Non-medical exposures	
Backscatter scanner for airport screening[12]	0.0008
One way flight, Helsinki to New York	0.05
Miner or nuclear industry worker (typical annual)	2
Background radiation to public (annual, worldwide[13])	2.4
Average annual limit, radiation workers[14]	20
Lifetime occupational radiation limit (Germany[15])	400
Non-cardiac medical imaging	
Chest X-ray	0.02
Mammogram	0.7
Head CT	2
Abdominal CT	10
Nuclear cardiology	
Low-dose technetium-99 m stress-only (450 MBq)	3
One day rest-stress or stress-rest technetium-99 m (450/1350 MBq)	13
Two day technetium-99 m (750/750 MBq)	11
Thallium rest-redistribution (92 MBq)	11
Dual isotope (US protocol) (120 MBq Tl/1110 MBq Tc-99 m)	22
F-18 Fluorodeoxyglucose (275 MBq)	5
Rubidium-82 rest-stress (1665/1665 MBq)	2
N-13 Ammonia rest-stress (555/555 MBq)	2
O-15 Water rest-stress (500/500 MBq)	1
Cardiac CT	
Calcium scoring	
Electron beam CT	1
Multidetector-row CT	3
Coronary CT angiography	
Prospectively triggered, 100 kVp	2
Prospectively triggered, 120 kVp	3
Retrospectively gated, ESTCM, 120 kVp	14
Retrospectively gated, 120 kVp	20
Cardiac catheterization	
Diagnostic catheterization	7
Percutaneous coronary intervention	20

ESTCM, electrocardiographically synchronized tube current modulation. Doses from nuclear cardiology procedures were estimated using EANM/ESC standard activities when available,[11] except for O-15 water where lower activities are now used with 3D acquisition, and the most recent International Commission on Radiological Protection tissue weighting factors[5] and dose coefficients,[16] with the exception of rubidium-82, for which more recent data suggest a lower effective dose.[17–19]

What evidence is there that levels of radiation received by cardiology patients can increase cancer risks?

Several large epidemiological studies suggest that exposure to low levels of radiation (<50 mSv effective dose), comparable with those received by many cardiology patients, is associated with a slightly increased risk of cancer (Table 3).

The best studied low-dose cohort is the Japanese atomic bomb survivor cohort. The Life Span Study, an extensive effort supported jointly by the Japanese and American governments, characterized patients by estimating radiation dose to the colon, which is comparable with effective dose to the whole body given the relatively uniform radiation exposure received by atomic bomb survivors. The 'exposed' cohort was defined as individuals receiving doses ≥5 mSv, while the 'non-exposed' cohort was defined as individuals receiving doses <5 mSv. Sixty-five per cent of the exposed cohort received radiation doses between 5 and 100 mSv. In this subgroup, with a mean dose of 29 mSv, 4406 solid cancers were observed between 1958 and 1998, an excess of 81 solid cancers over the

Table 3 Large epidemiological studies of low-dose (<50 mSv) radiation exposure

Population	Study	Study design	Sample size	Typical dose (mSv)	Excess relative risk of cancer[a]
Atomic bomb survivors	Life span study[23]	Cohort	105 427	29	0.02
Radiation workers	15-country study[24,25]	Cohort	407 391	19.4	0.02
In utero X-ray exposure	Oxford survey of childhood cancer[26]	Case–control	30 552	10	0.39

[a]At typical dose. $P < 0.05$ for each.

number that would have been expected based on cancer rates in the non-exposed cohort. This corresponds to an excess relative risk of 2% for the patients with doses of 5–100 mSv.[23] Similarly, the 15-country study of over 400 000 radiation workers, who were exposed to a mean dose of 19.4 mSv, observed an excess relative risk of 0.97 cancers per Sv (95% confidence interval; 0.14–1.97). For a dose of 19.4 mSv, this translates to an excess relative risk of 0.0194*0.97 or ~2% as well.

None of these large studies involved medically exposed adult cohorts. Several case–control studies, most notably the Oxford Survey of Childhood Cancer, have evaluated the relationship between low-dose *in utero* X-ray exposure and childhood cancers, and these have demonstrated a significant increase in cancer in exposed individuals.[26] Additionally, numerous smaller studies with higher typical radiation doses have studied adults receiving medical radiation exposures. These have included cohorts of patients receiving repeated chest fluoroscopies for tuberculosis treatment, therapeutic X-rays for treatment of mastitis, thymic enlargement, benign breast disease,[27] and ankylosing spondylitis,[28] external gamma rays for hemangioma,[27] and radiation therapy for a variety of malignancies.[29,30] While most of these studies demonstrated an increase in cancer rates with radiation exposure, some did not.[31]

A challenge, then, is that no simple model consistently describes the excess radiation-related cancer risks in each one of these cohorts.[27] Nevertheless, on review of the radiation epidemiology literature, the leading international advisory organizations,[13,32] as well as most but not all[33] national advisory organizations, have considered a linear no-threshold model as the simple model that best fits the existing data. Such a model implies that at low doses, cancer risk increases linearly with radiation dose, and that there is no dose below which there is no cancer risk. Our understanding of radiation epidemiology will be greatly enhanced by the results of several large epidemiological studies now studying cancer risks related to paediatric CT examinations. Together, these will follow over a million individuals exposed to computed tomography, and a meta-analysis is planned by the World Health Organization's International Agency for Research on Cancer. There is a need for further epidemiological research specifically focusing on patients undergoing cardiac imaging.

How can cancer risk from cardiac imaging be quantified?

Using data from the radiation epidemiology literature, it is possible to construct models relating radiation exposure to the lifetime attributable risk of cancer incidence or mortality. The models most widely applied currently are those developed in the US National Academies' Biological Effects of Ionizing Radiation (BEIR) VII report.[34] These models were developed by a panel composed of international experts in radiation epidemiology based upon exhaustive efforts, including comprehensive review of the pertinent world literature, input from many stakeholders, and review by another expert panel.[35] They are based largely on data from the Life Span Study, although they also incorporate data from medical radiation exposures. BEIR VII models have been applied to estimates of cancer risk from coronary CT angiography,[35,36] calcium scoring,[37] and myocardial perfusion imaging.[38] In general, the higher a patient's age, the lower the cancer risk; overall risks to women are greater than those to men; and the higher the radiation dose of a procedure, the higher the estimated risk. Estimated risks from a single imaging procedure have ranged from <1 in 10 000 for a low-dose study such as a calcium score or PET perfusion study performed in an elderly patient,[38] to nearly 1 in 100 for a high-dose coronary CT angiogram performed without dose reduction measures in a young woman.[35]

What are the limitations of such risk estimates?

The BEIR VII risk models are based upon numerous assumptions. The linear no-threshold model is used for risk estimation. There are, however, poorly understood biological mechanisms via which cancer risk may be in actuality greater or less than that suggested by a linear no-threshold model. These include the bystander effect, in which a DNA damage response is induced in non-irradiated cells that neighbour irradiated cells, and adaptive responses, whereby an initial exposure to radiation may 'prime' a cell, resulting in reduced biological effects from a second dose of radiation.[39] Furthermore, the only patient-specific information incorporated into these models is age and gender, and thus risk estimates do not reflect the myriad patient-specific factors that affect risk, such as comorbidities and risk factors.[40] Rather, such risk estimates reflect the risk to an actuarially typical member of a population undergoing a dosimetrically typical scan. Thus when applying such risk estimates to clinical scenarios involving patients with cardiovascular disease, it is important to keep in mind that calculated risk estimates may be overestimates, and mentally adjust the risk side of the benefit-risk balance accordingly. The BEIR VII models were developed for the US population although they can be straightforwardly adapted to other populations as well.[36]

Other uncertainties and assumptions in BEIR risk estimates relate to the methodology used to apply risk from a Japanese to an American population, which has differing patterns of cancer incidence and mortality, sampling issues related to parameter estimates, the value chosen for a factor used to compensate for the dose and dose rate of radiation received, and accounting for differences in potential for radiation damage between X-rays and other types of ionizing radiation.

What are the fundamental principles of radiation protection of patients?

The international system of radiation protection has two fundamental principles which apply to all sources of radiation. The *principle of justification* states that any decision that affects the existing radiation exposure situation, be that by introducing a new radiation source or reducing an existing exposure, should do more good than harm by achieving sufficient individual or societal benefit to offset the detriment it causes. The *principle of optimization of protection* states that the probability of incurring radiation exposures, the number of individuals exposed, and the magnitude of their doses should all be kept as low as reasonably achievable (ALARA), while accounting for societal and economic factors. This means that radiological protection should be the best possible under the circumstances, to maximize the margin of benefit over harm.[5,41] Notably, limits on radiation doses to an individual, while serving as a third fundamental principle of radiation protection for most planned exposure situations, are *not* appropriate for medical radiation, where such limits would often do more harm than good.

What tools do we have to assist in justification?

The main issue in Justification is whether a test is clinically indicated for a specific patient. There are several approaches by which test indications and their appropriate use can be evaluated. These include European guidelines published by the European Society of Cardiology, the guidelines by the American Heart Association and American College of Cardiology, and the Appropriateness Criteria published by the American College of Cardiology in conjunction with several other professional organizations.[42] These documents aim to identify those patients who are likely to gain benefit from a specific imaging test and in whom the expected benefit outweighs the harms. Although these indications are based on the clinical evidence of the accuracy of the tests and the usefulness of the information derived from the tests, consideration has also been given to the risks of the tests, including the risk due to ionizing radiation.

A detailed analysis of the accepted indications of the tests in each clinical scenario is beyond the scope of this review. However, the most obvious issue in Justification is to use imaging tests only in patients with accepted indications., E.g. in European Guidelines for on Myocardial Revascularization[43] none of the imaging tests is recommended in asymptomatic patients and in patients with stable angina but low pretest likelihood of coronary artery disease. Also, routine repeat testing is discouraged.

Despite providing important information about the use of medical imaging tests, these documents do not include all patient-specific information. In addition, the Appropriateness Criteria have been initially organized around specific imaging modalities rather than around specific populations of patients. These documents still leave the clinician a lot of responsibility in terms of what is the best test for an individual patient. These documents do not replace the analysis of the benefits and risks of each approach, including the option not to perform an imaging test.

What tools do we have to assist in optimization?

Many modality-specific approaches can be used to minimize the magnitude of radiation doses from cardiac imaging. These are summarized in Table 4.

How can benefits and risks of radiation be compared?

In general, selection of the 'right test for the right patient at the right time' involves evaluating the strengths and weakness of all diagnostic testing options, both inherent and as locally implemented. Clinical decisions should not be based solely upon radiation considerations, and estimated radiation-related risks can be weighted against the risk of undetected disease. To better understand the scale of risks, this risk can be also compared with other common risks of life. For example, the 10-year risk of death due to cardiovascular disease of an asymptomatic 50–60-year-old male with more than one risk factor for atherosclerosis is ~100 per 1000.[45] At this age, the lifetime increased risk of cancer due to radiation caused by a low-dose cardiac imaging test, such as a prospectively gated coronary CT angiogram, or PET or low-activitity stress-only sestamibi nuclear stress test, is on the order of 0.2 per 1000, i.e. 0.2% of the 10-year risk of cardiovascular death in the asymptomatic patient with risk factors. Correspondingly, if such an imaging study could prevent 0.2% of the deaths by cardiovascular diseases, this would counterbalance the risk of radiation. Even so, this does not preclude the need to optimize imaging protocols to keep radiation dose and cancer risk as low as reasonably achievable.

It is important to emphasize that the calculations above were based on an asymptomatic European population in which imaging tests are actually not even recommended. In the symptomatic population, the risk of cardiovascular disease should be considerably higher and it is easier to gain the relative benefit from testing. Futhermore, this analysis takes into account only cardiac mortalities during the following 10 years, while the risk of radiation in terms of fatal and non-fatal cancers is lifetime and primarily occurring after a latency period of 5–10 years. One should keep in mind, however, that for women, radiation risk is greater while cardiovascular risk is less, and for less optimized protocols, such

Table 4 Approaches to minimizing radiation dose from cardiac imaging (modified from Einstein *et al.*[44])

Computed tomography (CT)
When possible (especially with low heart rate, regular rhythm) employ scan modes that minimize time X-ray tube is on, and time X-ray tube is on at full current
Prospectively triggered
Step-and-shoot
Volume
High-pitch helical
Retrospectively gated with ECG-controlled tube current modulation
Use beta-blockers to lower heart rate
Minimize scan length
Match tube voltage and current to patient habitus; consider 100 kVp for non-obese patients
Consider avoidance of coronary CT angiography if calcium scoring scan reveals widespread, heavy coronary calcification
SPECT/PET
^{99m}Tc agents preferred when possible in SPECT
Consider stress-first/stress-only protocol for patients with low pretest probability
Minimize activity (mCi) to that needed to obtain good image quality with high degree of confidence
Consider lower activity (MBq) in smaller patients
For CT attenuation correction, minimize tube current
Hydrate after imaging and encourage early micturition
PET perfusion agents generally dosimetrically superior to SPECT agents
Fluoroscopy
Employ slowest fluoroscopy and fluorography frame rates that maintain diagnostic image quality
Minimize fluoroscopy and fluorography time
Use least amount of image magnification needed for accurate interpretation
Minimize distance from patient to image detector and X-ray tube
Optimize beam collimation
Minimize number of views
Shield sensitive organs, e.g. gonads
Use highest acceptable kilovolts to maintain lowest possible milliamphere
Omit left ventriculography if the diagnostic information is available from other tests

as helical CT angiography or dual isotope stress testing, radiation risk can be an order of magnitude or more greater.

Despite these estimations which suggest that for appropriately selected patients the benefits of imaging outweigh the risks due to radiation, one needs to recognize that there are limited randomized data documenting the benefit of the use of imaging tests. It is obvious that the expected benefits of the tests are lower in patients in whom the tests are not indicated. Several recent studies from the USA have observed 14–22% of cardiac imaging tests to have been performed inappropriately.[46–48] There are no such data from Europe but generally imaging has been clearly underused in Europe when compared with the USA, e.g. the use of SPECT perfusion imaging in European countries ranged from 500 to 3000 studies per million population in 2005,[49] while the corresponding number in the USA was 31 000.[50] Despite low absolute numbers in Europe, SPECT perfusion imaging was clearly the most commonly used of any non-invasive test for coronary heart disease. Thus, it is likely that imaging tests are not generally overused in Europe; rather the very low ratio (0.4) of non-invasive tests to invasive tests performed[49] suggests that non-invasive tests should in many patient populations be used more commonly.

Does radiation matter?

As demonstrated above, there is epidemiological data supportive of an increased risk of cancer incidence at levels of radiation commonly received by cardiac imaging patients. Cancer risk estimates deriving from this data, while limited by numerous assumptions and uncertainties, suggest that risk is small but from some cardiac imaging procedures non-trivial. There exist internationally accepted principles of radiation protection, namely justification and optimization, designed to optimize the balance of benefits and risks from radiation, and specific tools available to implement these principles in the context of cardiac imaging. Thus, while radiation should by no means be the sole or even the most important consideration in cardiac imaging, certainly radiation *does* matter.

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