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*REVIEW*

# Computed tomography and patient risk: Facts, perceptions and uncertainties

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## Abstract

Since its introduction in the 1970s, computed tomography (CT) has revolutionized diagnostic decision-making. One of the major concerns associated with the widespread use of CT is the associated increased radiation exposure incurred by patients. The link between ionizing radiation and the subsequent development of neoplasia has been largely based on extrapolating data from studies of survivors of the atomic bombs dropped in Japan in 1945 and on assessments of the increased relative risk of neoplasia in those occupationally exposed to radiation within the nuclear industry. However, the association between exposure to low-dose radiation from diagnostic imaging examinations and oncogenesis remains unclear. With improved technology, significant advances have already been achieved with regards to radiation dose reduction. There are several dose optimization strategies available that may be readily employed including omitting unnecessary images at the ends of acquired series, minimizing the number of phases acquired, and the use of automated exposure control as opposed to fixed tube current techniques. In addition, new image reconstruction techniques that reduce radiation dose have been developed in recent years with promising results. These techniques use iterative reconstruction algorithms to attain diagnostic quality images with reduced image noise at lower radiation doses.

**Key words:** Computed tomography; Radiation dose; Iterative reconstruction; Neoplasia; Carcinogenesis



**Core tip:** The rapid increase in computed tomography (CT) utilisation has brought with it significant public concern with regards to the doses of ionising radiation delivered during scanning due to the fact that some experimental and epidemiological evidence has linked exposure to low-dose radiation to the development of solid organ cancers and leukaemia. It now seems that a threshold-model of risk might be more appropriate with the risk increasing exponentially once cumulative doses of 100 mSv or more are reached. Nevertheless, there is an inherent responsibility on the medical community to keep radiation doses "as low as reasonably achievable". Each imaging procedure needs to be justified and optimised and the minimum radiation dose possible used to obtain a diagnostic CT should remain the goal in each clinical scenario.

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## INTRODUCTION

Since its introduction in the 1970s, computed tomography (CT) has revolutionized diagnostic decision making[1,2]. It has resulted in better surgery, better diagnosis and treatment of cancer, better treatment after injury and major trauma, better treatment of stroke and better treatment of cardiac conditions[3,4]. CT has many advantages over other imaging modalities in that it can be performed in minutes and is widely available which can allow physicians to rapidly confirm or exclude a diagnosis with improved conviction. It has had a major impact on the field of surgery where it has decreased the need for emergency surgery from 13% to 5% and has almost made many exploratory surgical procedures extinct. The widespread uptake of CT in clinical practice has been shown to decrease the proportion of patients requiring inpatient admission[5,6]. The progressive year on year technological advances in CT have also helped to make it an increasingly appealing imaging modality with higher spatial resolution and shorter scanning times leading to vastly increased number of clinical applications, *e.g.*, CT colonography, CT angiography, CT urography, *etc.*

Given these advantages, it is no surprise that CT has seen an explosion in its utilization since its inception[7]. In 2007, it was estimated that around 62 million CT scans were being obtained each year in the United States, compared with around 3 million per year in 1980[8]. One of the major concerns associated with the widespread uptake of CT is the associated increased radiation exposure incurred by patients. A United States study in 2009 found that CT is now responsible for 75.4% of the effective radiation dose delivered from all imaging procedures, while it accounts for only 11% of X-ray based examinations[9]. This increased reliance on CT scanning has resulted in the cumulative per-capita effective radiation dose received from medical imaging in the United States to increase almost six-fold between the years 1980-2006[10] (from 0.5 mSv to 3.0 mSv) and medical imaging is now the largest source of radiation exposure to humans other than natural background radiation[11] (in 2009, it contributed to over 24% of the United States population's radiation dose)[12]. Since

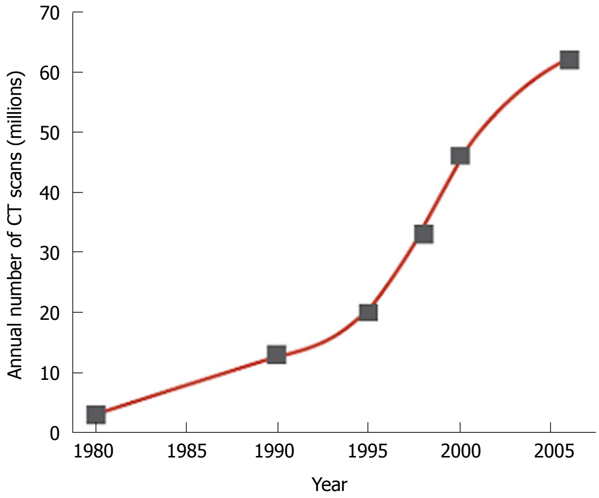


**Figure 1 Estimated number of computed tomography scans performed annually in the United States (Image directly from ref.[22]).** CT: Computed tomography.

the mid-1990's there has been an annual increase of almost 10% in the utilization of CT scanning[7]. The rapid expansion in the utilization of fluoroscopic and interventional radiologic procedures has also helped to contribute to the increases in ionizing radiation delivered by the medical community[13,14]. Combine these guided procedures with the potential advent of CT-based screening programs (*e.g.*, CT colonography[15], CT lung screening[16]) and there is an expectation that the reliance on CT scanning could continue to increase further in years ahead (Figure 1). This reliance on CT scanning is often further exacerbated by a lack of alternative imaging modalities, especially in smaller centres[17].

## RADIATION EXPOSURE AND CANCER RISK WITH CT SCANNING

The rapid increase in CT utilisation has brought with it significant public concern[18] with regards to the doses of ionising radiation delivered during scanning given that some experimental and epidemiologic evidence has linked exposure to low-dose radiation to the development of solid organ cancers and leukaemia[19]. It is widely accepted that large doses of ionising radiation increase the likelihood that an individual will go on to develop cancer during their lifetime but the association between low-dose radiation (of the order used in standard diagnostic examinations) and oncogenesis is unclear. The link between radiation and the subsequent development of neoplasia has been largely based on extrapolating data from studies of survivors of the atomic bombs dropped in Japan in 1945[20] and on assessments of the increased relative risk of neoplasia in those occupationally exposed to radiation within the nuclear industry[21]. Using this method of extrapolation where small hypothetical risks are multiplied by huge patient numbers, Brenner *et al*[22] estimated that in the future 1%-2% of all cancers in the United States would occur secondary to the effects of ionising radiation delivered by medical imaging, while a similar study by Berrington de González *et al*[23] in 2009 predicted that 29000 additional cancers and 14500 additional deaths could be expected each year.

While there is little dispute that large exposures to ionizing radiation such as are seen in nuclear disasters place an individual at an exponentially increased risk of developing cancer (analysis of the fall-out from the Chernobyl disaster has also highlighted an increased risk in thyroid cancer in those children exposed in utero downwind of Chernobyl)[24] there is widespread disagreement as to level of cumulative radiation dose delivered by medical imaging which increases the risk of cancer. While many authors argue that a linear no-threshold (LNT) model applies to the association between radiation and oncogenesis[22,25,26] others argue that a practical threshold exists below which the risks of cancer are no greater than an individual's background spontaneous risk[27,28]. A recent report has even suggested that exposure of individuals to low-dose radiation may elevate the immune response and thereby protect the individual from cancer, a concept known as hormesis[29,30]. The assertion that radiation induces cancer is a very broad statement. Particular organ systems are distinctly radiosensitive while others have more robust defences against the effects of ionising radiation. For example, organs such as the oesophagus, breast and bladder are particularly susceptible while organs such as the rectum, pancreas and prostate are much less sensitive[31].

The validity of the linear no-threshold model has come under even further scrutiny in more recent times[32]. An analysis of the Radiation Effects Research Foundation (REFR) data (which has followed the victims of the Hiroshima and Nagaskai attacks) compared cancer incidence in these cities with other Japanese cities which were not affected by the nuclear bombings. The group specifically looked at the incidence of colon cancer (commonly used as a cancer indicator in the Japanese population) and found that its incidence was not increased in those who received doses of radiation less than about 100 mSv[25]. It is suggested that ascribing cancer risks to radiation exposures of less than 100 mSv is confounded by other risk factors for malignancy within an individual population[28]. The REFR data was more consistent with the threshold-quadratic model of radiation-induced cancer than with a LNT model. Another issue in extrapolating experience of atomic bomb survivors in Japan to those exposed to ionising radiation in the medical setting is the inherent baseline differences in cancer risk amongst Japanese individuals *vs* populations of a different ethnic distribution (for example, stomach cancer is 10 times more prevalent in the Japanese community compared with United States subject, while breast cancer is three times more prevalent in the United States than in Japan)[25].

The linear-no-threshold model was initially adopted to assess radiation risk not because it has a solid biological and scientific foundation but because of its simplicity and its conservative nature (*i.e.,* the model is more likely to over-predict rather than under-predict the neoplastic risk associated with imaging)[33]. As far back as 1946, when Muller accepted his Nobel Prize for his work investigating genetic mutations in *Drosphilia* generated by the effects of X-ray (proposing the LNT model as a basis for predicting oncogenesis), there has been disagreement with regards to this model[34]. International societies are beginning to doubt its validity. The Health Physics Society concluded that at doses below 50-100 mSv "risks of health effects are either too small to be observed or are non-existent"[35]. The American Association of Physicists in Medicine supported this view stating that at dosages less than 50 mSv for single procedures and less than 100 mSv for multiple procedures the "predictions of hypothetical cancer incidence and deaths in patient populations exposed to such low doses are highly speculative and should be discouraged". Most tellingly, the United Nations Scientific Committee on the Effects of Atomic Radiation, one of the foremost international authorities on the effects of radiation in health, have also supported this position and have detailed that "statistically significant elevations in risk are observed at doses of 100 to 200 mGy and above" and that at dose ranges less than this no definitive risk can be ascribed to ionising radiation[31]. Doses of ionizing radiation delivered by common radiological procedures are outlined in Table 1[36].

While previously it had been insisted that even low doses of radiation were associated with risk of oncogenesis with a linear increase in risk with increased exposure, it now seems that a threshold-model of risk might be more appropriate with the risk increasing exponentially once cumulative doses of 100 mSv or more are reached[37]. This, however does not negate the danger associated with radiation or allow complacency when deciding on the validity of an indication for a particular scan. In patients with long-term chronic medical conditions, for instance, the requirement for repeated imaging makes them more likely candidates for incurring radiation exposure in the range of > 100 mSv. In a study of Crohn's patients (this patient subgroup have an increased risk of small bowel lymphoma at baseline)[38] over a 15-year period, it was shown that 16% of these patients had radiation exposure of > 75 mSv[39] and a similar study assessing maintenance haemodialysis patients found that 13% of this population experienced a cumulative dose of > 75 mSv over a median follow-up of 3.4 years[40]. In critically ill trauma patients the cumulative effective dose delivered to each patient averages 106 ± 59 mSv[41] (although in this patient group the risks of avoiding imaging usually far outweigh the potential risk of future malignancy). Given that most CT studies can average at two to three imaging phases per study the doses incurred by each

**Table 1 Doses of common radiological procedures**

| Examination | Average effective dose (mSv) | Values reported in literature |
|---|---|---|
| Posterioranterior study of chest | 0.02 | 0.007-0.05 |
| Head CT | 2 | 0.9-4.0 |
| Thorax CT | 7 | 4.0-18.0 |
| CT Pulmonary angiogram | 15 | 13.0-40.0 |
| Abdomen CT | 8 | 3.5-25 |
| Pelvic CT | 6 | 3.3-10 |
| Coronary angiography | 16 | 5.0-32 |

Annual effective dose from natural background radiation = 3 mSv. CT: Computed tomography.

individual exam can quickly accumulate, especially in the patient with chronic medical complaints requiring ongoing radiologic investigation.

## PAEDIATRIC AND FETAL SPECIFIC ISSUES

A simple dismissal of the linear-no-threshold model has engendered controversy since the recent publication of prospective data involving a large cohort study of paediatric patients in the United Kingdom who had undergone at least once CT scan between 1985 and 2002, when they were younger than 22 years of age. This data, albeit within the paediatric population, has been the first to suggest that medical imaging and the associated radiation exposure does indeed predispose to the development of cancer[42] and that the link is not just a speculative one based on extrapolation from prior disasters or occupational exposure in the nuclear industry. Pearce *et al*[42] and his team highlighted a linear association between the radiation dose to the brain and brain tumour risk and a similar association between doses received by the bone marrow and the development of leukaemia[43,44]. The authors chose to follow the incidence of these tumours following radiation therapy as these have been the malignancies which have been observed in irradiated children. These data were validated by the work of Mathews *et al*[45] who found a 24% increase in cancer incidence in a paediatric population exposed to a CT scan at least one year before a cancer diagnosis and followed up for 9.5 years. While these reports have helped to clarify the situation in the paediatric population the effects of radiation exposure in the adult population is less clear and whether or not this data can be directly applied to adult patients is ambiguous given that: (1) for any given CT examination, the doses delivered to adults is smaller than their paediatric counterparts[46,47]. The effective dose delivered to a neonate when assessing a particular anatomic site can be double those which an adult will receive for the same investigation[48]; and (2) children have been shown to have an inherently higher sensitivity to the effects of ionising radiation[20,48,49].

What is particularly concerning about the findings of these investigators is that it is within the paediatric population the expansion in CT utilisation is increasing at the most significant rate[50,51]. For example, between the years of 1991-1994 there was an increase of 63% in the utilisation of CT examinations in children less than 15 years of age[52]. This has been driven by a decrease in the scanning time for CT which reduces the need for sedation in younger or uncooperative children[53]. Conversely, despite the risks of radiation exposure in this sensitive cohort, the use of CT has had dramatic benefits in the paediatric population. Between 1990-2007, the expansion in utilisation of CT decreased the negative appendectomy rate from 23% to 1.7% with an associated decrease in the number of operations performed[54].

While the dangers of radiation exposure in the extremely young have been highlighted by recent population studies the situation with regard to the foetus in pregnant patients remains uncertain. While physicians have been demonstrated to have a poor understanding regarding the risks of imaging in pregnancy[55,56], this is likely due to the fact that there is no solid scientific evidence regarding the exact dangers. Data in animal studies has demonstrated teratogenicity but the doses used in these studies were much higher than those used in diagnostic scanning[57]. Studies of individuals exposed in utero at Hiroshima and Nagasaki have demonstrated growth restriction, microcephaly, mental retardation and increased risk of seizures from high dose radiation exposure[58,59]. While protocols exist which direct the need for scanning in pregnant or potentially pregnant patients these are primarily based on the linear no-threshold model rather than a specifically defined carcinogenic risk[60-62]. These protocols advocate minimising the radiation dose to which the foetus is exposed and concentrating the dose on the anatomy of interest; for example in suspected appendicitis, the scan volume should be restricted to include only potentially diagnostic areas and dual pass studies should be avoided[63,64]. Clearly, the use of imaging in pregnancy and particularly the use of CT always evokes enormous anxiety and is usually met with reluctance among radiologists and radiographers/radiology technologists. However, as in all clinical situations balancing of risk *vs* benefit is required based on best available evidence and considering how diagnostic information which may be gained by imaging may change management and improve clinical outcome *vs* potential risk to fetus and mother as a result of radiation exposure. The use of ultra-low dose protocols in pregnancy is therefore vital, until higher level evidence is available to inform decisions regarding imaging in pregnancy.

## PERCEPTION OF RISK ASSOCIATED WITH DIAGNOSTIC SCANNING

### *Patient perception*

While we know that ionising radiation confers certain risks to a patient, news media can sensationalise and exaggerate the potential adverse effects of radiation on carcinogenicity[65] which can induce anxiety in patients, particularly parents of children undergoing investigation[66,67]. In most instances the benefits of performing CT completely outweigh the potential risks. Medical doctors are increasingly encountering difficult situations when patients refuse CT scanning in clinical scenarios when CT scanning is clearly required; an example of this would be when a patient with newly diagnosed cancer who requires a CT for staging, declines the exam based on perceived risks associated with radiation exposure. Despite media coverage, patient understanding of the exact risks associated with CT scanning can, at times, be poor. Popular media have a tendency to focus on perceived and sometimes sensationalized dangers associated with radiation exposure associated with CT scanning while ignoring the enormous benefits in terms of expeditious and accurate diagnosis. Occasionally, excessive focus or lack of balance in the reporting of very rare incidences of error leading to extremely excessive radiation exposures from CT scanning as happened when it was discovered that one centre had been erroneously exposing patients to radiation doses eight times of normal during CT perfusion scanning[68].

On the other hand, patients have been shown to underestimate the relative amount of radiation delivered by CT scanning and, surprisingly given media coverage, underestimate the carcinogenic potential of exposure to ionizing radiation. In fact, one study has shown that patients will often have a higher degree of faith in their treating physician if they undergo computed tomography scanning as part of their work-up[69].

There is no question that there is a requirement for better patient education by imaging providers prior to the performance of CT scans. For example, it has been shown that 93% of adults referred for abdominal CT did not receive any information regarding the potential risks of this procedure and that only 3% of adult emergency patients are even aware of the potential association between CT and carcinogenesis[70]. Despite the inherent risks associated with paediatric CT[71] there is often reluctance on the part of physicians to convey the dangers associated with radiation for fear of confusing or upsetting parents with this information[72]. Striking a balance is difficult as the exact risk associated with radiation exposure in the range associated with CT scanning to patients, and particularly in children is unclear. However, informing parents about the slight risks associated with CT has not been shown to affect their willingness to allow their child to undergo scanning[73]. A balanced discussion of risks *vs* benefits with parents about the risks is paramount[74,75] as pressure is often exerted on physicians by parents encouraging the utilisation of CT in order to expedite diagnosis[76], without a thorough awareness of the dangers associated with this scanning. There is a need for multidisciplinary discussion involving experts in many disciplines (including radiology, radiation biology, medical physicist, public health physicians) so that a consensus can be agreed to guide physicians in providing advise to patients of varying ages with regard to risk associated with CT scanning. Proper counselling and education can help parents become more willing to accept a more conservative strategy[73]. Despite limited knowledge amongst some physicians regarding the carcinogenic potential of CT scanning there are concerted efforts amongst radiologists and physicists to reduce radiation exposure through imaging to patients. Using newer technologies, and strategies such as iterative reconstruction, radiation exposures associated with CT scanning are diminishing incrementally[77].

## PHYSICIAN AND MEDICAL STUDENT PERCEPTION

Difficulty arises when balancing the immediate need for diagnosis with the unlikely potential for harm associated with a CT scan. To this effect, there tends to be a reliance on the individual health care providers to be cognisant of potential dangers and to minimize patient exposure to "as low as reasonably achievable". There can be a lack of recognition from health care workers, however, regarding potential dangers associated with CT. A United States study of health care providers found that less than 50% of radiologists and only 9% of emergency department personnel were aware that there was a potential association between CT and the development of malignancy[70]. Data have also shown that many physicians are also unaware of the doses of radiation associated with individual examinations[78,79]. A systematic review on physicians' knowledge of radiation exposure and risk found that there was often a "low level of knowledge and radiation risk awareness"[80]. An assessment of American paediatric surgeons found that 53% of all respondents thought that the lifetime risk of cancer was increased from exposure to one abdomino-pelvic CT scan, although 75% underestimated the dose delivered by this scan compared with a chest X-ray. The report also found that the majority of paediatric surgeons did not discuss the potential risks associated with these scans with their patients[81].

Poor physician awareness has also been observed in the United Kingdom and other parts of the EU[79], where appreciation of the consequences of radiation exposures was similar to the United States with most underestimating the dose of radiation delivered by common radiological investigations[78,82]. Similarly, in an Australian cohort of doctors, it has been shown that the "knowledge of radiation exposure from medical imaging is poor[83]". It has also been highlighted that not only is there deficient knowledge amongst doctors regarding radiation dose incurred through imaging but that radiation dose is often not considered to be an important consideration when referring for radiological investigation[84]. The reasons why there is such a poor understanding amongst clinicians regarding the dangers associated with radiation could be explained by a lack of training at undergraduate and postgraduate level[85]. It has clearly been shown that there is a lack of awareness at undergraduate level[86].

Research in the postgraduate population has found that there is often limited focus on radiation safety and radiation protection within training programmes and have highlighted the importance of increased education initiatives in this area, both within radiology and other specialities[87]. Teaching of radiology at an undergraduate level and delivery of dedicated radiation protection education improves student's awareness.

## DOSE REDUCTION STRATEGIES

While we may not be certain as to the exact oncogenic potential of ionising radiation there is an inherent responsibility on the medical community to keep radiation doses "as low as reasonably achievable (ALARA)". Each imaging procedure needs to be justified and optimised and the minimum radiation dose possible used to obtain a diagnostic CT should remain the goal in each clinical scenario. With improved technology, significant advances have already been achieved with regards to radiation dose reduction. The dosage delivered from a combined CT study of the abdomen and pelvis has declined by a factor of between two and three since the 1980s due to a number of different technological innovations[88]. However despite these technological advances and emphasis on the ALARA principle, radiation exposure has been shown to vary over a tenfold range in clinical practice for the same investigation, depending on variable parameters[23]. This type of variation can exist both within and between different institutions with wide discrepancies in average dose reported[89]. While standards and limits exist for health care workers and those routinely exposed to radiation occupationally (*e.g.*, nuclear workers) there is currently no legal requirement for routine monitoring of cumulative effective radiation dose which patients may be exposed to during the diagnostic process[90-92].

Integration of hospital PACS systems on a national and international level would help to allow cumulative radiation exposure for each patient to be tracked. This type of database is currently being developed by the scanning industry (GE healthcare's Dosewatch® system being an example of this). These platforms also allow optimisation tools which can be utilised by both radiographers and radiologists to try to minimise radiation exposure while, at the same time, maximising the clinical information which will be attained by each scan and limiting the risk of duplicating scans which have already been carried out at other institutions. Defined exposure limits can be stipulated for each type of scan and the technology will inform the physician if these pre-defined limits are exceeded. This would also allow departments the opportunity to audit and streamline their practices. Also, this online collection of radiation dose data associated with imaging procedures, will alert individual departments to sporadic incidences of high radiation exposures and allow immediate action to prevent large cohorts of patients from suffering very high radiation exposures as a result of diagnostic imaging.

Scanning techniques can be optimally adjusted (Table 2) in order to try to achieve an acceptable image at lower exposure level. Dose reduction can be achieved *via* a wide variety of means[93] as below.

**Table 2 Methods to try to optimise dose delivered during computed tomography scanning[3]**

| Current dose reduction strategies in CT scanning | Dose reduction strategies gaining interest[92] |
|---|---|
| Solid state scintillating detectors | Manual/automated adjustment of scanner output according to patient size *via*:<br>Tube current modulation;<br>Selection of the most dose-efficient tube potential |
| Electronic circuits with lower levels of background noise | Iterative reconstruction methods |
| Multi-detector row arrays | Increased spiral pitch or non-spiral methods in cardiac CT |
| More powerful X-ray tubes and generators | |
| Beam shaping filters which vary the X-ray intensity across the patient cross section | |

CT: Computed tomography.

### *Tube current modulation and automatic exposure control[94]*

Different patients, depending on their size, will all require different radiation doses and the most basic feature which can be modulated in each patient is the tube current[76]. For example, the amperage utilised in paediatric scanning should be significantly lower than that utilised in their adult counterparts[95] (and needs to be higher in obese patients). The tube current should be modulated based on the overall attenuation of the anatomic area being assessed[96]. Other techniques, such as ECG based current modulation can be used to help reduce the dose during cardiac CT[94,97]. Automatic exposure control, is a relatively new technique, which modulates the tube current during an individual scan based on the different attenuations of different anatomic regions. This also has the added advantage of delivering the optimal dose to achieve the optimal diagnostic image[98]. Radiologists can define the quantity of noise, which is acceptable to individual clinical scenarios, prior to the scan thus aiding the difficult task of balancing of image quality and radiation exposure.

Strategies to design an ideal tube potential for individual patient sizes and different diagnostic tasks have been published and these have been demonstrated to reduce doses by 70% for the chest and by 40% for the abdomen[99]. In the case of cardiac CT, electrocardiographic based tube current modulation can allow doses to be reduced by levels of between 30%-90%[97]. Further advances using a dual source CT system allows dose reductions by a factor of up to 10-12[100].

### Iterative reconstruction

Iterative reconstruction has been one of the most significant advances in dose reduction technology in CT scanning in recent times. This type of technology, when used in conjunction with or in place of filtered back projection, may improve noise and spatial qualities within the image[101]. Iterative reconstruction techniques allows images of improved quality to be acquired at significantly lower radiation doses[102]. As technology and software continues to improve it is likely that iterative reconstruction algorithms will progress concurrently[103].

### Noise reduction filters

This technique has the potential to optimise quality of acquired image by eliminating noise and have been demonstrated to substantially reduce radiation dose[104,105].

### Low dose protocols[106,107]

Low dose strategies for abdominal CT scanning in children and young adults have been shown to be non-inferior to standard dose CT with respect to negative appendectomy rates[108,109]. These low dose strategies can use up to four times less radiation than the standard dose protocol.

### Spacing of CT slices

Using a large number of thin adjacent CT slices can result in significant increases in radiation dose to the patient. Multi-slice CT scanners also deliver considerably more radiation dose due to scan overlap, positioning of the CT scanner in closer proximity to the patient and increased scatter radiation[110]. There is therefore an important balance to be met when selecting a slice small enough to achieve the optimal diagnostic image and large enough to ensure that the radiation dose delivered is acceptable[111].

### Maintaining the limits of radiation field within anatomy of interest

All too often during image acquisition in CT the area being scanned includes extra images which are outside the field of original interest. For example, one study found that when assessing the utilisation of abdomino-pelvic CTs that extra images above the diaphragm were obtained in 97% of cases and that images below the symphysis pubis were obtained in 94% of patients[112]. This equated to an additional 1280 images in 106 patients and while the images provided additional radiation exposure in each patient there was little additional diagnostic information in the majority of these cases. Maintaining the field to only the area of interest can allow smaller cumulative dosing and potentially improved images *via* focused imaging[113].

### Decision support at the time of ordering a scan

Automated prompts and advice as part of online radiology ordering systems can help to reduce the number of low utility examinations carried out[114] (one study demonstrated that this type of system can reduce the number of low utility examinations threefold)[115].

### Split bolus techniques for urological studies

Typical CT urography protocols have required multiple image acquisitions to obtain the unenhanced, contrast-enhanced nephrographic, and contrast-enhanced excretory phase images. This method of multiple image acquisition requires a significant radiation burden (quoted between 15-35 mSv)[116,117]. However, the utilisation of split bolus protocols can significantly reduce this burden and exposes the patient to doses similar to that experienced in standard unenhanced and contrast enhanced abdomino-pelvic CT[118].

### Virtual non contrast CT from dual energy CT

**Rational scanning:** The strategies outlined above can play a huge role in minimising the dose administered to the patient during various scanning procedures. However, the best dose reduction strategy is to avoid needless scanning. Unfortunately, it has been shown that large numbers of scans are undertaken each year which are lacking in a valid clinical indication[119]. In fact, it has been suggested that perhaps 20%-40% of all CT scans could be avoided if decisions to scan were based on available guidelines[120,121]. In the paediatric population it has been shown that one third of all CT scans could be replaced by alternative approaches or not performed at all[122] and questions have also been raised regarding the routine use of CT for diagnosing appendicitis within the same population, despite its impressive results in reducing negative appendectomy rates[123]. There is scope for replacing or reducing CT in favour of other diagnostic modalities. Magnetic resonance imaging and ultrasound have the benefit of not exposing the patient to any ionizing radiation but their utility is compromised by availability [in the case of magnetic resonance imaging (MRI)][124,125] and image quality (in the case of ultrasound[126]. Also in some clinical scenarios, MRI does not offer equivalent diagnostic information when compared to CT. Decision support software programmes which rate the appropriateness of a CT scan as it is ordered by a physician, are difficult to develop, but have shown impressive reductions in the expansion of CT scanning[114]. Given that between 20%-40% of CT scans are ordered inappropriately as per evidence based guidelines[127], the introduction of these types of initiatives to encourage physicians to re-assess the clinical necessity for each scan is encouraging. The American College of Radiologists have recognised the need for thorough guidelines to assist physicians in deciding when particular scans should be utilised[128]. However, a caveat to the introduction of these types of decision support is that the application of a no-denial policy on radiological imaging, surprisingly, did not result in increased utilisation of imaging modalities[129].

Of course when imaging is clinically indicated then the benefit-risk balance is almost always overwhelmingly in favour of imaging[128,130]. However, all too often the decision to image is based on time constraints, medico-legal concerns or patient preference. There is, as yet, no study which attempts to quantify and assess the risk-benefit ratio for radiological investigations and responsibility lies with the referring physician and radiologist[131]. The need to optimise clinical decision making with regards to imaging therefore needs to be guideline based as this alone has the potential to reduce the influence of convenience factors[132]. The risk/benefit ratio is individual to each patient. The following factors contribute to oncogenic risk from radiation.

**Genetic considerations**: Certain populations and individuals may be more radiosensitive and have more of a propensity to develop cancers post radiation exposure[133]. For example, some patient groups with a genetic abnormality which predisposes to cancer have been shown to be more sensitive to the effects of radiation[134,135].

**Age at exposure**: The BEIR Ⅶ report demonstrated the relationship between the life-time attributable risk of cancer incidence and age at exposure, showing that the risks of carcinogenesis was much higher the earlier that patient was exposed to high doses of radiation[21]. Older patients undergo the majority of medical imaging but limited life expectancy reduces risk of radiation induced cancers[21]. Criteria for imaging in these patients should not necessarily be the same as for those for younger patients with curable disease[136]. The longer post-radiation life expectancy in the paediatric population allows greater scope for the generation of malignancy and this fact has been borne out by recent population based studies from the United Kingdom[42] and Australia[45].

**Sex**: There appears to be a trend towards a higher incidence of cancer in females post exposure to radiation as opposed to men (even with similar exposures to radiation)[137].

**Illness**: Many patients who undergo repeated imaging while being treated for illness likely to reduce life expectancy. Oncogenic effects of this imaging radiation are unlikely to to materialise[136].

**Fractionation and protraction of exposure**: In general, it is believed that there is a greater risk from high doses of radiation delivered over a short time period in comparison with the same (or lower doses) delivered over a protracted course due to the influence of DNA damage repair[138]. However, the influence of the cumulative dose being delivered over a longer period has been suggested to be, surprisingly, small[139,140].

The reality is that rational scanning will rely on the appropriate knowledge base amongst physicians and trainees. Therefore, the role of education of medical staff, both at undergraduate, postgraduate and even more senior level cannot be underestimated given the shortcomings in knowledge of radiation exposure identified above. These types of educational initiatives have previously shown to be successful in reducing scanning numbers when implemented appropriately[141].

## CT SCANNING: RECOMMENDATIONS FOR THE FUTURE

Clarity regarding the association between radiation exposure and oncogenesis is, as yet, not fully elucidated. However, despite this, the goal when imaging patients should always be to use a dose that is "as low as reasonably achievable". Imaging, irrespective of the risk, should only be used when the potential clinical benefit outweighs the potential risk. The three fundamental principles of radiation which are laid out by the International Commission of Radiologic Protection include[142]: (1) justification; (2) dose optimization; and (3) dose limitation.

There is a responsibility to adhere to these fundamental principles. Given that it has been shown that low-dose protocols do not impact diagnostic yield, such protocols need to become the standard[108]. Recent data has shown that a single scan has low risk but given CT expansion cumulative doses can escalate. The extrapolation of small carcinogenic risks in the individual to cumulative cancer figures in the population is often sensationalized by the popular media resulting in significant distress and anxiety amongst the public, which can make patients and their families reluctant to undergo scans which may be in their best interests.

The future of radiation optimisation will include education of physicians and patients. Such initiatives include the Image Gently® and Image Wisely® campaigns. Image Gently® provides information regarding paediatric population radiation safety to parents and physicians and guides dose optimisation[143,144]. The Image Wisely® campaign promotes radiation safety in the adult population and has developed an honour roll for facilities and associations who have pledged to "image wisely" within their practice[145]. The Image Gently® initiative has been further developed to include specific guidance on paediatric interventional procedures under the title of Step Lightly®[146,147], In response to the Cedar-Sinai controversy in the United States, the Food and Drug Administration has also launched a national initiative to reduce unnecessary radiation exposure to patients[148]. It is apparent that physicians are not effectively discussing the potential risks of radiation exposure with their patients, however small[149]. When potential radiation dose exposure is substantial, for example, during interventional procedures, radiation risk needs to be a component of consent prior to the procedure. With increased prevalence of radiologic investigations, patient education regarding the risks of radiation exposure needs to be tackled by the medical community in order to accurately convey potential risk. The Interventional Radiology Patient Safety Program among others have issued guidelines resulting in practice modifications where excessive radiation doses were being delivered intra-procedurally[150,151]. Incorporating audit as standard into radiology departments can also help to decrease the dose delivered to each patient[152,153] and will also help when discussing these scans with our patients. The establishment of national reference levels for specific CT examinations will allow audit at a local, national and international level[154-157]. While controversy still exists regarding the exact oncogenic risk associated with CT scanning simply ignoring the issue is not acceptable but audit, education and reassessment are key to improved understanding and safer practices.

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ORIGINAL ARTICLE

Retrospective Study

# Value of serial magnetic resonance imaging in the assessment of brain metastases volume control during stereotactic radiosurgery

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## Abstract

***AIM***

To evaluate brain metastases volume control capabilities of stereotactic radiosurgery (SRS) through serial magnetic resonance (MR) imaging follow-up.

***METHODS***

MR examinations of 54 brain metastases in 31 patients before and after SRS were reviewed. Patients were included in this study if they had a pre-treatment MR examination and serial follow-up MR examinations at 6 wk, 9 wk, 12 wk, and 12 mo after SRS. The metastasis volume change was categorized at each follow-up as increased (> 20% of the initial volume), stable (± 20% of the initial volume) or decreased (< 20% of the initial volume).

***RESULTS***

A local tumor control with a significant ($P$ < 0.05) volume decrease was observed in 25 metastases at 6-wk follow-up. Not significant volume change was observed in 23 metastases and a significant volume increase was observed in 6 metastases. At 9-wk follow-up, 15 out of 25 metastases that decreased in size at 6 wk had a transient tumor volume increase, followed by tumor regression at 12 wk. At 12-wk follow-up there was a significant reduction in volume in 45 metastases, and a significant volume increase in 4 metastases. At 12-mo follow-up, 19 metastases increased significantly in size (up to 41% of the initial volume). Volume tumor reduction was correlated to histopathologic subtype.

*CONCLUSION*

SRS provided an effective local brain metastases volume control that was demonstrated at follow-up MR imaging.

**Key words:** Brain metastases; Stereotactic radiosurgery; Magnetic resonance imaging; Pseudo-progression; Radiation therapy



**Core tip:** Stereotactic radiosurgery (SRS) provided an effective long-term local volume control of brain metastases during 12-mo magnetic resonance (MR) imaging follow-up. A significant reduction of the tumor volume by 6 wk post-SRS was associated with long-term volume control suggesting that the timing for MR imaging follow-up at 6 wk, 9 wk, 12 wk and 12 mo after SRS, could be considered the most effective to provide useful information to make the best treatment decisions.

Sparacia G, Agnello F, Banco A, Bencivinni F, Anastasi A, Giordano G, Taibbi A, Galia M, Bartolotta TV. Value of serial magnetic resonance imaging in the assessment of brain metastases volume control during stereotactic radiosurgery. *World J Radiol* 2016; 8(12): 916-921 Available from: URL: http://www.wjgnet.com/1949-8470/full/v8/i12/916.htm DOI: http://dx.doi.org/10.4329/wjr.v8.i12.916

## INTRODUCTION

Brain metastases account for 20%-40% of adult cancer and affect survival and quality of life[1]. The two most commonly used treatments for brain metastases are whole-brain radiation therapy and stereotactic radiosurgery (SRS), which extend survival from 3 mo to 5 mo and from 7 mo to 13 mo, respectively, depending on tumor type. Surgical resection remains a valuable approach for patients with larger symptomatic metastatic tumors[2].

SRS is an increasingly used procedure for the treatment of primary and metastatic intracranial brain tumors. Indications include patients with few, well-defined, and small intracranial brain tumors. In SRS, radiations are directly delivered into a brain tumor, thus reducing radiation dose of surrounding normal brain tissue and side effects such as neurotoxicity, skin damage, nausea and vomiting[3-5]. The damage to the peritumoral brain is further reduced by a step dose gradient at the target periphery of the tumor[3].

The objectives of SRS include local tumor control, defined as the absence of a substantial (< 25%) increase in tumor volume at follow-up magnetic resonance (MR) imaging, improved quality of life, and prolonged survival[6,8]. Metastatic lesions are particularly well-suited for the treatment with SRS because they are usually small (< 3 cm), well-circumscribed, and have well-defined margins[6].

Studies have demonstrated that SRS is an effective alternative to traditional surgical resection and whole brain radiotherapy in patients with single or few well-defined brain metastases[1,7-9].

Knowledge of natural history of brain metastases treated with SRS is crucial to prevent management dilemmas, and reduce patient anxiety. For instance, radiation toxicity can sometimes cause a pseudo-progression of brain metastases, which usually resolves with time[1,7,9,10].

The purpose of this study is to evaluate volume tumor control capabilities of SRS in the treatment of brain metastases trough serial MR imaging follow-up.

## MATERIALS AND METHODS

### *Patient population*

This was a retrospective study approved by the Institutional Review Board of our institution. All patients were referenced with the diagnosis of brain metastases and were treated with Gamma Knife-SRS (Leksell Gamma Knife, model 4C, GammaPlan 5.3; Elekta Instruments, Stockholm, Sweden) at a single academic medical center from January 2015 to January 2016. All patients had given written consent for this retrospective study. Patients were included in this study if they had a pre-treatment MR examination and serial follow-up MR examinations within 6 wk, 9 wk, 12 wk, and 12 mo post-SRS.

Patients were excluded if SRS was performed for consolidation to a surgical resection bed only. Additionally, patients in whom lesions required salvage surgery due to symptomatic local failure, were excluded.

The SRS dose delivered to the tumor margins ranged from 18 to 24 Gy prescribed to the 40%-70% isodose surface. Radioresistant tumors (melanoma, renal cancer) received a median marginal dose of 23.7 Gy (range, 20-24 Gy), and radiosensitive tumors (lung and, breast cancer) received a median marginal dose of 21.3 Gy (range, 18-24 Gy).

There was a total of 31 patients (14 men, 17 women; age: 32-77 years; mean age, 51, 5 years) that underwent serial MR imaging examinations at 6 wk, 9 wk, 12 wk, and 12 mo after SRS.

Brain metastases were confirmed by pathology.

**Table 1 Patient population and primary cancer types**

| No. of patients | Gender | Age (yr) | Primary cancer type | No. of lesions, (%) |
|---|---|---|---|---|
| 11 | 7 men - 4 women | 50-70 | Non-small cell lung carcinoma | 19 (36) |
| 9 | 1 men - 8 women | 32-60 | Breast carcinoma | 16 (29) |
| 7 | 5 men - 2 women | 55-77 | Renal cell carcinoma | 9 (16) |
| 4 | 1 men - 3 women | 32-65 | Melanoma | 10 (19) |

There were 54 brain metastases: Non-small cell lung carcinoma *n* = 19 (36%), breast carcinoma *n* = 16 (29%), renal cell carcinoma *n* = 9 (16%), and melanoma *n* = 10 (19%). Patient population and primary cancer types are summarized in Table 1.

### MR imaging

All MR examinations were performed with a 1.5T MR scanner (Signa Excite, GE Medical Systems, Milwaukee, United States). MR imaging protocol included axial and sagittal fast spin-echo (FSE) T2W [5100/110 (TR/TE)] images, axial fluid-attenuated inversion-recovery (FLAIR) [8000/140/2400 (TR/TE/TI)] images, along with axial, sagittal, and coronal non-enhanced and contrast-enhanced (0.1 mmol/Kg gadobutrol - Gadovist, Bayer, Germany) FSE T1W [650/15 (TR/TE)] images with a FOV of 22 cm, matrix 512 × 512, slice thickness 5 mm, intersection gap 1 mm, number of excitations 2. Follow-up MR examinations were performed at 6 wk, 9 wk, 12 wk, and 12 mo post-SRS.

### Volume change analysis

Two experienced neuroradiologists evaluated in consensus the maximum enhancing metastasis volume measured in 3 orthogonal planes at initial MR examinations and at each follow-up. Tumor volume was calculated according to the following formula: Volume = length × width × height/2 as reported in other studies[7]. Metastases of at least 0.5 $cm^3$ were included. Metastasis volume change was categorized at each follow-up as increased (> 20% of the initial volume), stable (± 20% of the initial volume) or decreased (< 20% of the initial volume). This criteria was chosen taking in account a measurement error of 20%, as there are no validated categorization schemes for tumor response.

### Statistical analysis

Statistical analysis was performed using the statistical software package SPSS (SPSS, Chicago, Ill). The Wilcoxon signed-rank test for continuous variables was used to evaluate the significance of volume change. A multivariate logistic regression analysis was used to determine the correlation between histopathology and volume changes. A *P* value of < 0.05 was considered statistically significant.

## RESULTS

Primary cancer types and effective time point for MR imaging follow-up to identify significant phases of the response to the SRS therapy are summarized in Table 2. At 6-wk follow-up, a local tumor control with a significant volume decrease up of 63% was observed in 25 brain metastases (46%) (12 non-small cell lung carcinoma, 11 breast carcinoma, 1 renal cell carcinoma, 1 melanoma). No significant volume change was observed in 23 metastases (43%) (6 non-small cell lung carcinoma, 5 breast carcinoma, 7 renal cell carcinoma, 5 melanoma), and a significant volume increase was observed in 6 metastases (11%) (1 non-small cell lung carcinoma, 1 renal cell carcinoma, 4 melanoma).

At 9-wk follow-up, 15 out of 25 radiosensitive brain metastases (28% of the total lesions) (8 non-small cell lung cancer, 7 breast metastases) that decreased in size at 6 wk had a transient tumor volume increase, followed by tumor regression at 12 wk with no clinical symptoms (pseudo-progression) (Figure 1).

At 12-wk follow-up, there was a significant reduction in volume in 45 metastases (18 non-small cell lung carcinoma, 14 breast carcinoma, 7 renal cell carcinoma, 6 melanoma), no significant volume change in 5 metastases (1 non-small cell lung carcinoma, 1 breast carcinoma, 1 renal cell carcinoma, 2 melanoma), and a significant volume increase in 4 metastases (1 breast carcinoma, 1 renal cell carcinoma, 2 melanoma).

At 12-mo follow-up, 19 (35%) metastases increased (true-progression) significantly in size (up to 41% of the initial volume) (1 non-small cell lung cancer, 4 breast cancer, 6 renal cell carcinoma, 8 melanoma) (Figure 2).

The logistic regression analysis showed that volume tumor reduction correlates to histopathologic subtype: non-small cell lung carcinoma had a significant reduction of 38% of its initial volume; breast carcinoma had a significant reduction of 41% of its initial volume; renal cell carcinoma had a significant reduction of 14% of its initial volume; melanoma had a significant reduction of 8% of its initial volume. Thus, higher tumor reduction was observed in the radiation sensitive carcinomas (breast and non-small cell lung carcinomas).

Moreover, we evaluated the volume tumor variation of breast, non-small cell lung cancer, melanoma, and renal cell carcinoma metastases at 6 wk, 9 wk, 12 wk, and 12 mo post-SRS. Our results show that response categorization differences among these 4 primary types were not statistically significant, however melanoma and renal cell carcinoma metastases had less robust volume reduction than non-small cell lung cancer or breast metastases.

Temporary or permanent clinical complications were evaluated during 12 mo follow-up of these patients. Transient headache related to intracranial edema was noted in 10 patients, with nausea (5 patients) and arm or leg weakness (2 patients). Permanent neurologic

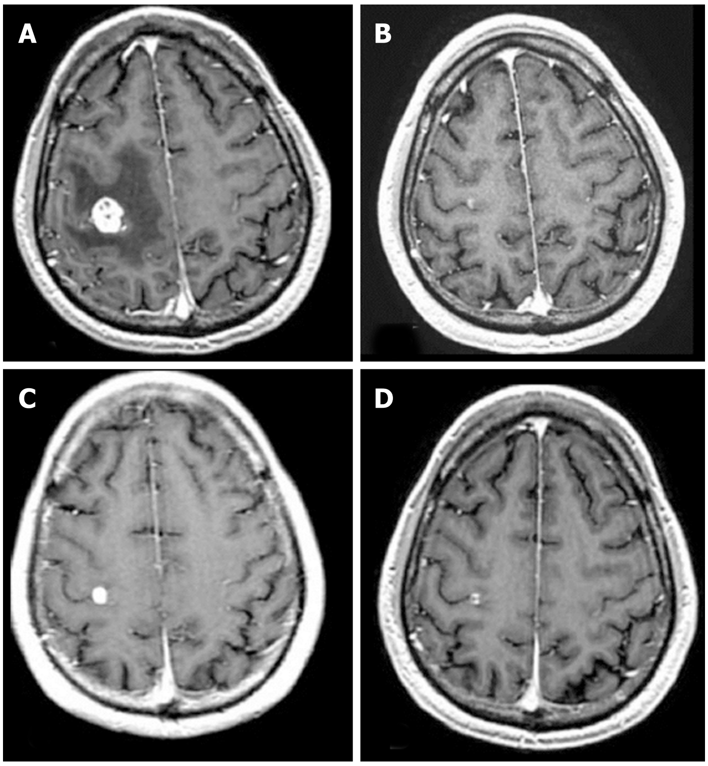


**Figure 1 Follow-up axial enhanced T1-weighted magnetic resonance images of a brain metastasis from breast carcinoma treated with stereotactic radiosurgery in a 60-year-old woman.** A: Pre stereotactic radiosurgery (SRS) magnetic resonance (MR) image; B: Initial follow-up MR image at 6 wk after SRS demonstrating an initial volume reduction; C: Follow-up MR image at 9 wk after SRS demonstrating a transient volume increase (pseudo-progression); D: Follow-up MR image at 12 wk demonstrating a final volume reduction.

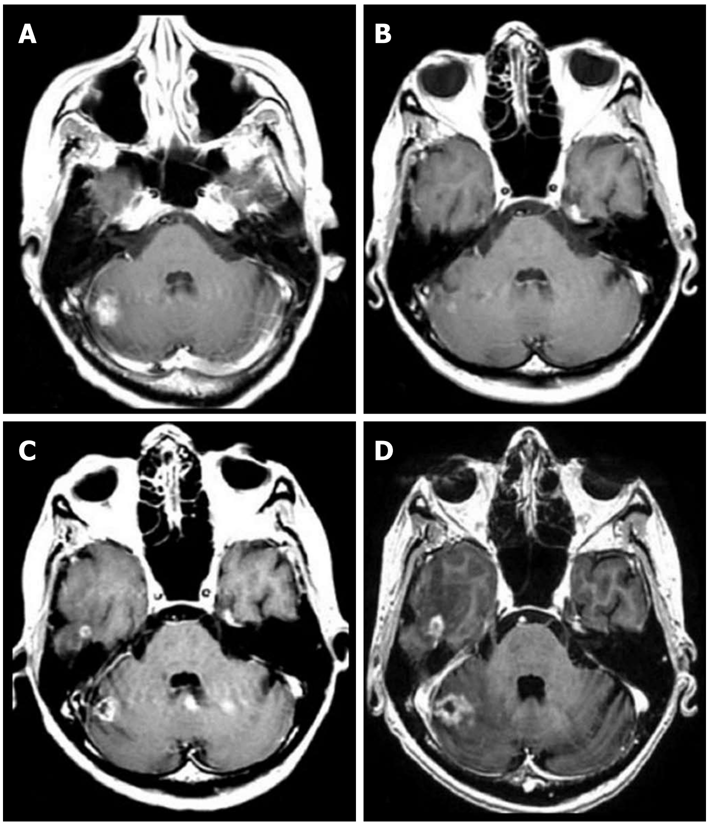


**Figure 2 Follow-up axial enhanced T1-weighted magnetic resonance images of a lung carcinoma metastatic to the right cerebellum treated with stereotactic radiosurgery.** A: Pre stereotactic radiosurgery (SRS) magnetic resonance (MR) image; B: Initial follow-up MR image at 6 wk after SRS demonstrating an initial volume reduction; C: Follow-up MR image at 9 wk demonstrating volume increase (true-progression); D: Follow-up MR image at 12 wk with final volume increase.

deficits were noted in 6 patients.

## DISCUSSION

Our results suggest that a significant early reduction of tumor volume is associated with a good long-term volume tumor control as reported in previous studies[6,7,10-14]. Conversely, increased tumor volume at 6-wk follow-up has a higher probability of a final increase in lesion size, thus in a poor tumor volume control.

Transient volume growth at 9-wk follow-up occurred in 15 radiosensitive brain metastases (8 non-small cell lung cancer, 7 breast metastases) (28% of the total lesions), followed by tumor regression at 12 wk with no

**Table 2 Primary cancer types and effective time point for magnetic resonance imaging follow-up to provide useful information for the treatment decision**

| Primary cancer type | No. of lesions | %[4] | Reduced in size at 6 wk[1] | %[4] | Pseudo-progression (9 wk)[2] | %[4] | True-progression (12 mo)[3] | %[4] |
|---|---|---|---|---|---|---|---|---|
| Non-small cell lung carcinoma | 19 | 36 | 12 | 22 | 8 | 15 | 1 | 2 |
| Breast carcinoma | 16 | 29 | 11 | 20 | 7 | 13 | 4 | 7 |
| Renal cell carcinoma | 9 | 16 | 1 | 2 | 0 | 0 | 6 | 11 |
| Melanoma | 10 | 19 | 1 | 2 | 0 | 0 | 8 | 15 |
| Total | 54 | 100 | 25 | 46 | 15 | 28 | 19 | 35 |

[1]Number of lesions reduced in size at 6-wk follow-up; [2]Number of lesions that presented a transient volume growth (pseudo-progression) at 9-wk follow-up; [3]Number of lesions that presented final volume growth (true-progression) at 12-mo follow-up; [4]Percentage of lesions computed over the total number of lesions ($n$ = 54).

clinical symptoms (Figure 1 and Table 2). This transient growth must be careful interpreted as it could be misinterpreted as tumor recurrence, whereas it should be interpreted as a pseudo-progression[7].

The histopathology of pseudo-progression is probably related to treatment-induced tumor inflammation and necrosis[7,10-13]. Tumor volume variation trend in our series demonstrates that melanoma and renal cell carcinoma metastases showed less volume reduction than non-small cell lung cancer or breast metastases.

However, response categorization differences among these 4 primary types were not statistically significant, thus suggesting that the most effective timing for MR imaging follow-up, regardless the type of primary tumor, could be considered at 6 wk, 9 wk, 12 wk and 12 mo after SRS.

The observation that a small percentage of lesions may undergo a transient volume increase indicate that initial lesion growth does not necessary preclude local volume control. Conversely, there were a low number of metastases that exhibited initial volume growth and continued to grow with no volume control during SRS (Figure 2).

SRS has become the standard procedure for the treatment of brain metastases as it allows a longer survival and higher local control rates compared to whole-brain radiation therapy[6,7,9,14]. Compared to surgical resection, SRS is associated to lower morbidity and decrease cost[1].

To summarize, SRS is effective in treating brain metastases regardless of their histology, including those that are radio-resistant to conventional whole-brain radiation therapy, such as metastases that originates from melanoma and renal cell carcinoma.

Although initial consistent tumor volume reduction after SRS is predictive of long term volume control, initial tumor growth does not necessarily indicate tumor progression but radiation-induced inflammation and necrosis (pseudo-progression) and it should be taken into account to avoid to be misinterpreted as a recurrence.

### *Limitations*

This study was a retrospective, single-institution study with a relative small size population and these factors could be considered limitations.

To prevent potential inaccuracies in the volume measurement of the intracranial lesion, we excluded lesions with an initial tumor volume of less than 0.5 $cm^3$ and a 20% cutoff for volume response categorization was chosen.

In conclusion, effective long-term SRS local volume control of brain metastases can be demonstrated at 12 mo follow-up. Significant tumor volume reduction by 6 wk post-SRS was associated with long-term volume control suggesting that the timing for MR imaging follow-up at 6 wk, 9 wk, 12 wk and 12 mo after SRS, could be considered the most effective to provide useful information to make the best treatment decisions. Although it is necessary to validate these results in a larger, prospective series, the results are encouraging that an early local volume reduction after SRS is associated with significant local control for metastatic brain lesions.

## COMMENTS

### *Background*

Brain metastases account for 20% to 40% of adult cancer and affect both survival and quality of life. Brain metastases volume reduction is associated with significant local control of the lesions and prolongation of patient's survival. Stereotactic radiosurgery (SRS) is an increasingly used procedure for the treatment of primary and metastatic intracranial brain tumors to achieve local volume reduction.

### *Research frontiers*

Volume tumor control capabilities of SRS in the treatment of brain metastases is an important factor for post-treatment decision making and delivery salvage therapy.

### *Innovations and breakthroughs*

Volume tumor control capabilities of SRS could be demonstrated trough serial magnetic resonance (MR) imaging follow-up. Accurate determination of the timing for MR imaging follow-up is crucial for decision making and delivery timely salvage therapy.

### *Applications*

Serial MR imaging follow-up at 6 wk, 9 wk, 12 wk, and 12 mo is the most effective timing to demonstrate volume reduction of brain metastases after SRS. The information derived from serial MR imaging follow-up could affect clinical management and improve survival of these patients.

### *Terminology*

SRS is a procedure for the treatment of primary and metastatic intracranial brain tumors. Indications include patients with few, well-defined, and small intracranial brain tumors. In SRS, radiations are directly delivered into a brain tumor, thus reducing radiation dose of surrounding normal brain tissue and side effects such as neurotoxicity, skin damage, nausea and vomiting. The damage to the peritumoral brain is further reduced by a step dose gradient at the target periphery of the tumor. The objectives of SRS include local tumor control, defined as the absence of a substantial (< 25%) increase in tumor volume at follow-up MR imaging, improved quality of life, and prolonged survival.

### *Peer-review*

This study is interesting. However the manuscript would be of higher value to the reader if the manuscript focuses on the pseudo-progression period, that period is confusing for the practicing physician and can lead to misinterpretation and additional or changes in treatment strategies.

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*ORIGINAL ARTICLE*

Observational Study

# Assessment of fetus during second trimester ultrasonography using HDlive software: What is its real application in the obstetrics clinical practice?

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## Abstract

***AIM***

To show imaging results from application of four-dimensional (4D) ultrasound lightening technique (HDlive™) in clinical obstetrics practice.

***METHODS***

Normal and abnormal fetuses at second and third trimester of pregnancy undergoing routine scan with 4D HDlive™ (5DUS) in the rendering mode are described. Realistic features of fetal structures were provided by 5DUS in the rendering mode. Normal anatomy as well as pathology like cleft lip, hypoplastic face, micrognathia, low-set ears, corpus callosum, arthrogryposis, aortic arch, left congenital diaphragmatic hernia are highlighted in this study. Anatomical details of the fetuses were provided by 5DUS with higher quality imaging modality compared to those obtained using conventional 2D/3D ultrasound.

***RESULTS***

Realistic views of fetal anatomy details were displayed by means of 5DUS in the rendering mode, with high image quality obtained either in low-risk or in high-risk obstetrics population. Corpus callosum, esophagus, and aortic arch were obtained in normal fetuses. Cleft lip, cleft lip and palate, micrognathia, hypoplastic face, low-set ears, arthrogryposis, left congenital diaphragmatic

hernia, exomphalos, and clitoris hypertrophy were clearly rendered by 5DUS application.

***CONCLUSION***
The use of 5DUS in the rendering mode, when clinical available, was diagnostic in a variety of congenital anomalies, aided understanding of the parents-to-be and improved prenatal counseling and perinatal management.

**Key words:** Three-dimensional ultrasound; Four-dimensional ultrasound; HDlive; Second trimester scan; Congenital anomalies



**Core tip:** Four-dimensional ultrasound using HDlive™ allows realistic images of fetal anatomic structures in the second trimester of pregnancy. These images allow identifying fine details of fetal surface, with better understanding both multidisciplinary team and parents.

Tonni G, Grisolia G, Santana EF, Araujo Júnior E. Assessment of fetus during second trimester ultrasonography using HDlive software: What is its real application in the obstetrics clinical practice? *World J Radiol* 2016; 8(12): 922-927 Available from: URL: http://www.wjgnet.com/1949-8470/full/v8/i12/922.htm DOI: http://dx.doi.org/10.4329/wjr.v8.i12.922

## INTRODUCTION

The second trimester scan, also called anomaly scan, is usually performed between 18-23 wk, and is based on a systematic anatomical survey of the fetus, placenta and umbilical cord, in order to detect possible fetal abnormalities[1]. The ultrasound examination should be carried out according to international standard[2] and possibly by accredited sonographers who have completed appropriate training program by scientific societies[3].

The sensitivity and specificity for detection of congenital anomalies by means of conventional 2D ultrasound may be estimated around 83.5% and 99.8%, respectively[4,5]. The technologic advancement gained by real-time, high definition three- and four-dimensional ultrasound (3D/4DUS), enable acquisition of volume that can be analysed online or offline by "navigating" within the volume in the three orthogonal planes. 3D/4DUS post-processing techniques allow anatomical details to be investigated in sagittal, axial and coronal planes, improving prenatal diagnosis of congenital malformations[6-8].

Hereafter, we present a pictorial editorial from normal and pathologic cases obtained during second and third trimester of pregnancy in low- and in high-risk pregnancy using 4D HDlive™ (5DUS) software.



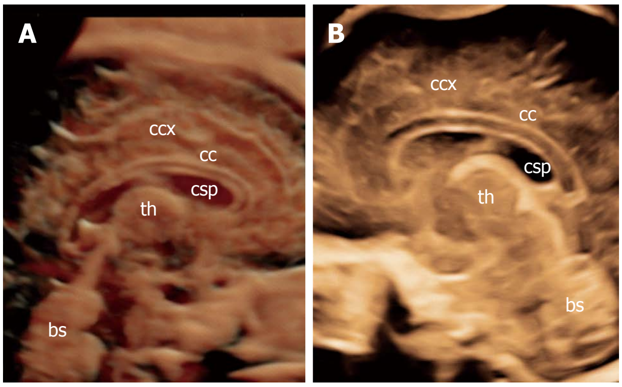


**Figure 1 Normal fetal brain at 28 wk of gestation.** A: 4DUS using HDlive™ shows, with impressive image quality resembling that of gross anatomy, the cerebral cortex (ccx), the corpus callosum (cc), the cavum septum pellucidum (csp), the thalamus (th) and brainstem (bs) in mid-sagittal plane; B: The same images using the conventional 3DUS in the rendering mode.

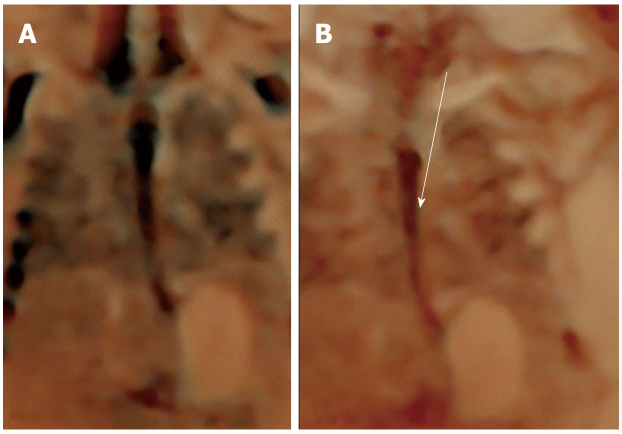


**Figure 2 Normal fetal esophagus at 28 wk of gestation.** A and B: 4DUS using HDlive™ application may be used to obtain a clear imaging of inner structure of esophagus (arrow) during fetal swallowing at the time of routine second trimester scan.

## MATERIALS AND METHODS

Ultrasound examinations were performed using Voluson E8 apparatus equipped with a transabdominal volumetric RAB4D ultrasound probe (GE, Milwaukee, WI). Fetal anatomical survey was performed using conventional 2D ultrasound, and 3D/4D HDlive™ (5DUS) applied both in low- and in high-risk pregnancy. The study was approved by the local Ethics Committee of both Guastalla Civil (AUSL Reggio Emilia) and "Carlo Poma" hospitals (AUSL Mantua), Italy. Four-hundred low-risk and seventy-six high-risk pregnant women entering the clinical trial gave written informed consent. Two consecutive volumes were acquired during transient maternal apnea and fetal rest to reduce motion artefacts. The sweep took less just than few seconds. Acquisition angle of 45-60 degree was used, depending on the gestational age. All 3DUS volumes were saved both onto the ultrasound equipment and onto a optical disk for post-processing analysis. 5DUS application was applied to the best 3DUS volume stored and different

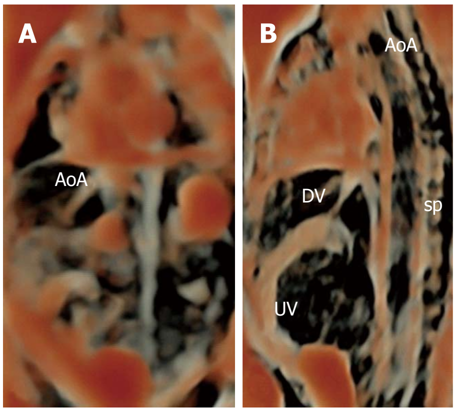


**Figure 3 Normal fetal aortic arch at 28 wk of gestation**. 4DUS echocardio-angiography using HDlive™ application to the study of the great artery and veins: the AoA (A, image is rotated), the UV and the DV (B) are rendered with an enhanced quality resembling that of an angiographic study (sp, fetal spine). AoA: Aortic arch; UV: Umbilical vein; DV: Ductus venosus; sp: Fetal spine.

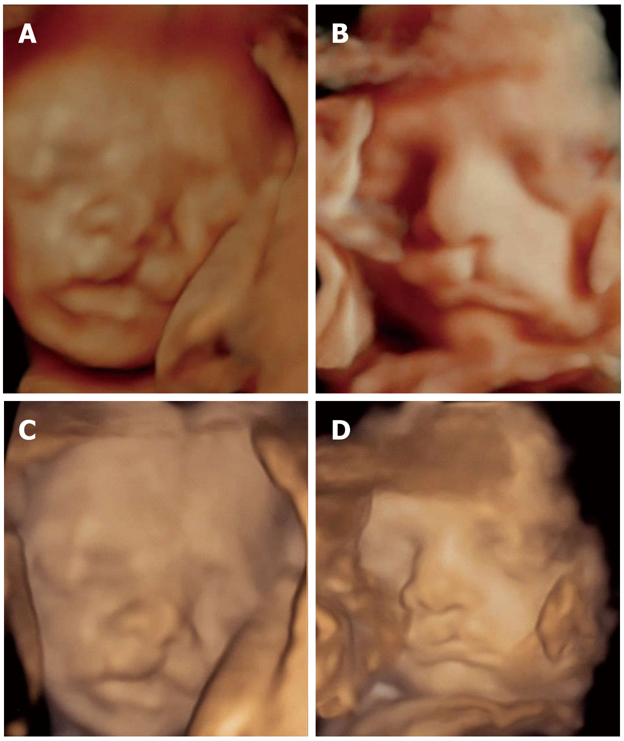


**Figure 4 4DUS using Hlive™ (5DUS) lightening technique: Realistic rendering in a case (A) of left-sided cleft lip and palate and left-sided cleft lip (B).** C and D: The same images using the conventional 3DUS in the rendering mode.

lightening and shadowing adjustments were made to obtain the highest image quality rendering. Offline analysis was performed using a computer developed platform (4DView™, Zipf, Austria); HDlive™ (5DUS) software was applied after uploading the software onto a personal computer using a freely released flash-drive pen.

## RESULTS

Realistic views of fetal anatomy details were displayed

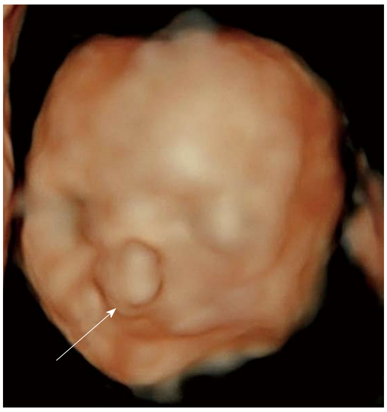

**Figure 5 4DUS using Hlive™ showing the right-sided cleft lip and palate (arrow) in a fetus with 21 wk-3 d.**

**Figure 6 4DUS using HDlive™: Micrognathia (arrow) is clearly rendered.**

**Figure 7 4DUS using HDlive™ showing a hypoplastic face.**

**Figure 8 4DUS using HDlive™ enabled a clear snapshot of low-set ears in this case detected at 24 wk of gestation.**

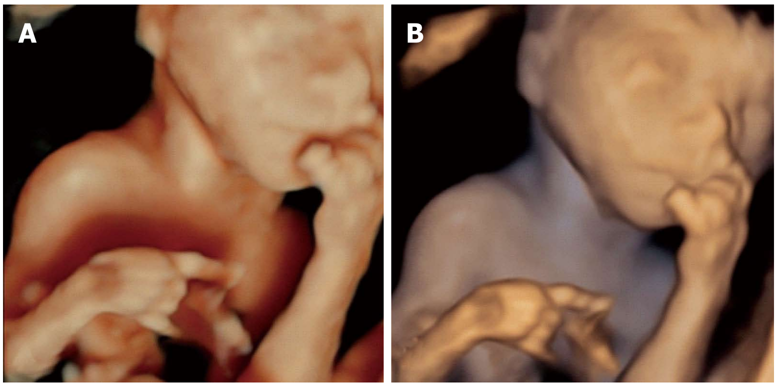


**Figure 9 Arthrogryposis multiplex congenital.** A: 4DUS using HDlive™, note the characteristic muscular contractions causing fingers deviation; B: The same using the conventional 3DUS in the rendering mode.

by means of 5DUS in the rendering mode, with high image quality obtained either in low-risk or in high-risk obstetrics population. Corpus callosum (Figure 1), esophagus (Figure 2), and aortic arch (Figure 3) were obtained in normal fetuses.

Cleft lip (Figure 4), cleft lip and palate (Figure 5), micrognathia (Figure 6), hypoplastic face (Figure 7), low-set ears (Figure 8), arthrogryposis (Figure 9), left congenital diaphragmatic hernia (Figure 10), exomphalos (Figure 11), and clitoris hypertrophy (Figure 12) were clearly rendered by 5DUS application.

## DISCUSSION

This pictorial editorial displays a gallery of normal and pathologic cases obtained during second and third trimester of pregnancy by means of 5DUS in the rendering mode. 3D/4DUS with its technical applications has resulted in improved diagnostic accuracy compared with conventional 2DUS, especially when applied to the field of fetal medicine, where high definition 3D/4DUS produces real-time reconstruction of the fetal anatomy[9-13]. HDlive™ imaging often looks like a picture taken inside the uterus[14] and may enable detection of subtle malformations that may go undiagnosed using conventional 2DUS. This may be particularly seen when dealing with surface abnormalities such as those involving the fetal face where 4DUS, especially with HDlive™ rendering mode, may offers a potential imaging enhancement. Previous observation has documented a role for 3DUS to provide additional information compared to 2DUS for the prenatal diagnosis of facial, skeletal and neural tube defect[15]. An extended review from Tonni *et al*[16] has described the technical advancements obtained over the past 20 years by 3D/4DUS compared to conventional 2DUS in different fields of application, particularly in prenatal diagnosis. The study of the fetal face, palate and detection rate of cleft lip and cleft palates has resulted enhanced when 3D/4DUS has complemented 2DUS, either in the first as in the second trimester of pregnancy[17-23]. Undoubtedly, one of the main advantages of 3D/4DUS is represented by the possibility of volume acquisition compared with "flat" images obtained by 2DUS. Once a volume is acquired, it can be further manipulate by "navigating" online or offline within the volume. In addition, anatomical details can be displayed in all the three orthogonal planes. Furthermore, 3D/4DUS can be used in training program as the volume can be freely section on demand and send to expert at remote site using DICOM (digital communication in medicine) technology[16]. Moreover, observations have shown that 4DUS has been a valuable diagnostic investigation to assess fetal neurobehavioral state as it allows visualization of yawning, sucking, smiling, and blinking activity[13,14]. 5DUS differs from conventional rendering methods because it uses a fixed virtual light source that calculates the propagation of light through skin and tissue. Operators can freely select the light source at any angle relative to the ultrasound volume to

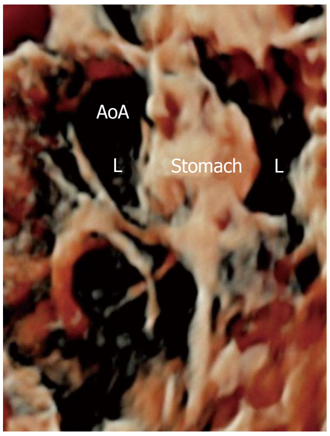


**Figure 10  4DUS using HDlive™ application in a case of left congenital diaphragmatic hernia.** AoA: Aortic arch; L: Lung.

**Figure 11  4DUS using HDlive™ application in a fetus with exomphalos (curved arrow) was diagnosed at early second trimester scan (15 wk-3 d).**

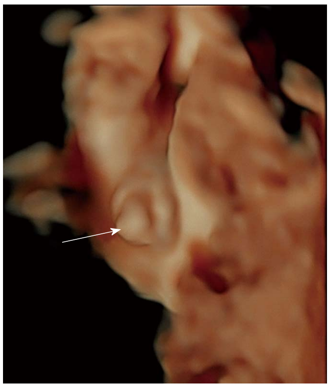

**Figure 12  4DUS using HDlive™ application in a case of clitoris hypertrophy (arrow) detected at 27 wk of gestation in an intersexual state (postnatal chromosomal assessment resulted in 46,XY karyotype).**

enhance anatomical details[11]. 5DUS is a relatively easy technique to be applied and does not require specific clinical training for operators already confident with post-processing 3D/4DUS techniques. The time needed to obtain online the desired reconstructed image and display it on the ultrasound screen can be estimated usually in about 1 minute, depending upon experience gained and anatomical details that need to be rendered. For comparison analysis of image quality between 3DUS *vs* 4D HDlive™, it is advisable to save and stored the 3DUS volumes on the ultrasound apparatus and to export them onto a flash-drive pen or onto an optical disk for further offline post-processing analysis. This is required because once HDlive™ is applied to a 3DUS volume, the rendered image will be saved automatically in this modality and previous 3DUS volume is lost. 5DUS may represents a complementary diagnostic tool to confirm fetal abnormalities and to characterize anatomical details such as those seen in rare syndromes thus improving accurate prenatal diagnosis, genetic counseling and antenatal management in targeted cases. Importantly, these "life-like" images provided by HDlive™ may represent a technological improvement in 3D imaging that may strengthen the maternal-fetal bonding process[24,25]. HDlive™ software has shown limitations in conditions of poor imaging quality, such as in cases of increased maternal body mass index, presence of abdominal scar or uterine myomata as well as fetal positioning *in utero*. In the current clinical trial, unsuccessful volume acquisition for adequate 4D HDlive™ rendering has occurred in 6.75% of cases in low-risk and 3.9% in high-risk pregnancies. However, some of these clinical limitations may be overwhelm by transvaginal approach. Nonetheless, further studies will be needed to assess the role of 5DUS and its clinical validation before the use of this advanced lightening software may be included in obstetrics practice and be used at the time of routine scan in low-risk women or applied to the study of structural fetal malformations in high-risk pregnancies.

## COMMENTS

### *Background*

The second trimester scan, also called anomaly scan, is usually performed between 18-23 wk, and is based on a systematic anatomical survey of the fetus, placenta and umbilical cord, in order to detect possible fetal abnormalities. The ultrasound examination should be carried out according to international standard and possibly by accredited sonographers who have completed appropriate training program by scientific societies. The sensitivity and specificity for detection of congenital anomalies by means of conventional 2D ultrasound may be estimated around 83.5% and 99.8%, respectively.

### *Research frontiers*

The technologic advancement gained by real-time, high definition three- and four-dimensional ultrasound (3D/4DUS), enable acquisition of volume that can be analysed online or offline by "navigating" within the volume in the three orthogonal planes. Previous observation has documented a role for 3DUS to provide additional information compared to 2DUS for the prenatal diagnosis of facial, skeletal and neural tube defect.

### *Innovations and breakthroughs*

The authors present a pictorial editorial from normal and pathologic cases obtained during second and third trimester of pregnancy in low- and in high-risk pregnancy using 4D HDlive™ (5DUS) software.

### *Applications*

3D/4DUS post-processing techniques allow anatomical details to be investigated in sagittal, axial and coronal planes, improving prenatal diagnosis of congenital malformations.

### *Peer-review*

Well written manuscript, nice pictures.

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CASE REPORT

# Horizontally root fractured teeth with pulpal vitality - two case reports

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## Abstract

This case study reports the successful outcome of horizontal root fractures of two different patients, which took place in permanent incisors. Report 1 describes a case of a 29-year-old patient who suffered a mandibular trauma affecting mainly the lower central incisors, caused by a car accident. A panoramic radiograph was taken right after the accident and showed a horizontal root fracture in the middle third of tooth 42, which went untreated. Report 2 illustrates a case of a 17-year-old male patient who searched for orthodontic therapy and the periapical radiograph showed horizontal root fracture in tooth 11 caused by a previous trauma, which went untreated as well. There was healing through the reestablishment of pulp activity and dental coloration without professional intervention.

**Key words:** Horizontal root fractures; Pulpal vitality; Periapical radiograph



**Core tip:** The innovative arguments of this paper is the importance of the follow up procedure conceding the biological response of each patient facing root fractures; especially apex remodeling, calcification and root resorptions. Dentists must be aware that such biological responses may happen without professional interference, which, made previously, might have a complete different outcome.

Silva L, Álvares P, Arruda JA, Silva LV, Rodrigues C, Sobral APV, Silveira M. Horizontally root fractured teeth with pulpal vitality - two case reports. *World J Radiol* 2016; 8(12): 928-932 Available from: URL: http://www.wjgnet.com/1949-8470/full/v8/i12/928.htm DOI: http://dx.doi.org/10.4329/wjr.v8.i12.928

## INTRODUCTION

Horizontal root fractures have been more frequently detected in the maxillary upper anterior region, affecting mainly the second life decade of the male patient group[1]. They usually occur in fully erupted teeth with complete root formation[2,3]; frequently seen in the middle third of the root followed by apical and coronal third fractures[4]. This paper aims to describe two cases of root fracture with pulpal vitality which healed without professional intervention.

## CASE REPORT

### *Case report 1*

A 29-year-old male patient searched for dental assistance on September 2009 for extraction of the tooth 42 by his own will. He had suffered a trauma caused by a car accident back in May 2008. A panoramic radiograph taken at the time of the accident showed a two fragment middle third horizontal root fracture in tooth 42 (Figure 1A). After intraoral examination, normal aspects were observed in tooth 42, including color, absence of mobility and positive response to pulp sensibility test (EndoFrost®) (Figure 1B and C); Tooth 41 was slightly grayish, responding negatively to sensibility test. Periapical radiograph (Figure 1D) and cone beam tomography showed hypodense image in the periapex in tooth 41. Tooth 42 showed a hypodense image in the middle third of the root confirming a fracture with no hypodense lesions in the periodontium. As the tooth 42 responded positively to pulp sensibility test, the hypodense line was interpreted as cicatricial fibrosis (Figure 2). Tooth 44 showed external dentinal root resorption plus remodeling of the apex, also showing a calcification spot in the apical third of the root canal, while tooth 43 had its apical third obliterated. The sensibility test to cold was negative. After the diagnosis the patient did not return for the accomplishment of the endodontic treatment.

### *Case report 2*

A 17-year-old male patient's periapical radiographic examination for orthodontic purposes showed a horizontal radiolucent line in the root of tooth 11, suggesting root fracture. The pulp chamber and the cervical third showed normal aspects, as well as the periapex. The patient reported trauma in the region back in 2006. In 2008 in a routine dental appointment the horizontal root fracture was then detected. The tooth was vital and thus a clinical and radiographic follow-up took place in September 2015. A cone beam tomography was then requested and confirmed horizontal root fracture in tooth 11 with fragments discreetly not aligned, showing no signs of resorption in the root and the periapical bone tissue around the fracture (Figure 3A). The root segments were juxtaposed and aligned in the mesio-distal direction (Figure 3B, D and F) and slightly misaligned in buccolingual direction (Figure 3C and D). In Figure 4, observed horizontally root fractured in the radiographic takings distoradial and ortoradial. Clinically, the tooth showed no crown mobility or discoloration and its vitality continued to be demonstrated by the sensibility test.

## DISCUSSION

The outcomes for traumatized teeth can be altered by many situations, such as the stage of root formation, periodontal conditions and trauma type and intensity. Normally, when the patients search for dental care in the case of a trauma, current literature instructs to immobilize the tooth with a semi-rigid splint for 4 wk up to 4 mo (Table 1)[5-9]. Sensibility tests, immediately performed in the post trauma, are not indicated since they might worsen the clinical condition after the accident[2,5].

It is also possible that, in the cases described in this paper, the connective tissue of the pulp has not been ruptured at all, although a cleavage has affected the root. Particularly in report 1, the initial radiograph suggests that the traumatized tooth was free of mechanical forces by the absence of the antagonist tooth. The apex was closed, and its potential entrance for blood vessels no longer existed. Therefore, the only possible entrance available was the connective tissue from the periodontal ligament accessed by the fracture.

A similar situation took place in report 2. The impact seems to have been greater so that the fragments became apart, and a new blood supply seems to have been independently formed in both fragments. Paradoxically, it was the fracture itself that was the likely responsible for the existence of an additional blood supply in both cases. Another interesting fact is that in both cases, the fractured teeth were not the main cause that made the patients visit the dentist. In report 1, tooth 41 was the one with the best prognosis, and had a final completely paradoxal outcome, presenting a periapical lesion and the need of endodontic treatment due to pulp necrosis. On the other hand, patient in report 2 had no complaint at all. It is worth mentioning that in both cases the teeth remained untreated and were not splinted[10].

The study of orthodontics combined with root fractured teeth orthodontic movement is crucial because pressure applied on traumatized teeth displays small risks of resorption when pulp condition is normal. However, whether treating or not teeth with root fractures is still an endodontic clinical dilemma[11].

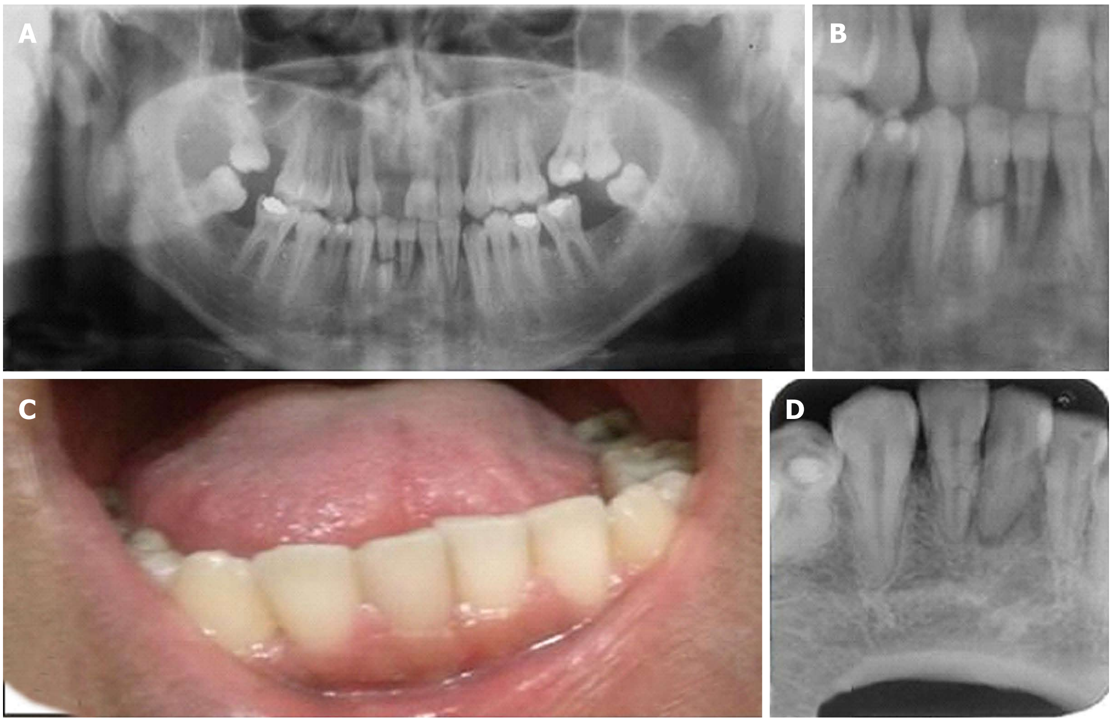


**Figure 1 Radiographic and clinical as immobilize the tooth with a semi-rigid splint for 4 wk up to 4 mo.** A: Panoramic radiograph taken at the moment of the accident; B: Close at the fractured tooth at the time of the accident; C: Intraoral view. Tooth 41 was slightly grayish while tooth 42 had normal color and no mobility was present; D: Periapical radiograph, tooth 41 with a radiolucent lesion compatible with periapical lesion; tooth 42 with a thin radiolucent line at the fractured line.

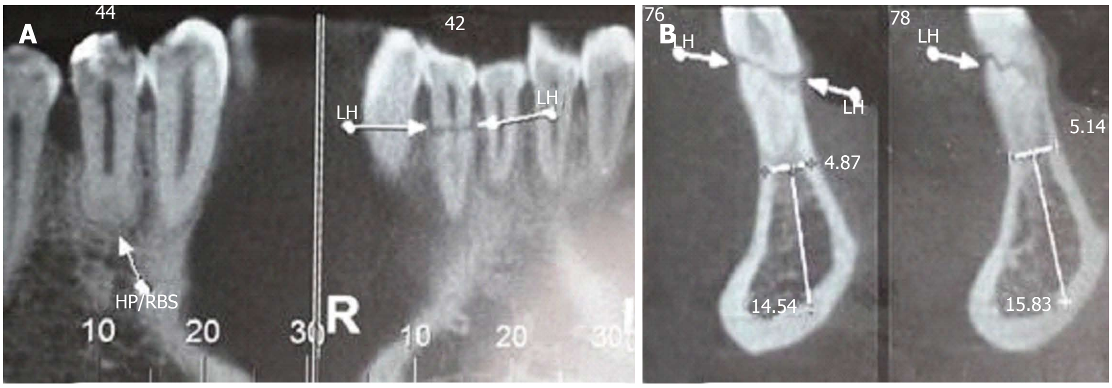


**Figure 2 Cone beam tomography images.** A: Cone beam computed tomography (CT) shows apex remodeling and root canal apical third obliteration of teeth 44 and 43, as well as fracture line in tooth 42; B: Cone beam CT shows oblique fracture line along the middle third of tooth 42. LH: Horizontal line.

**Table 1 Procedures Suggested by the American Association of Endodontics for fractured permanent teeth and alveolar fractures**

| Time | Root fracture | Alveolar fracture |
|---|---|---|
| 4 wk | Splint removal[1], clinical and radiographic control | Splint removal and clinical and radiographic controls |
| 6-8 wk | Clinical and radiographic control | Clinical and radiographic control |
| 4 mo | Splint removal[2] and radiographic control | Clinical and radiographic control |
| 6 mo | Clinical and radiographic control | Clinical and radiographic control |
| 1 yr | Clinical and radiographic control | Clinical and radiographic control |
| Yearly for 5 yr | Clinical and radiographic control | Clinical and radiographic control |

[1]Splint removal in apical third and mid root fractures; [2]Splint removal with a root fracture near the cervical area.

According to Brin *et al*[11] previously traumatized teeth are most prone to developing root resorptions, although in a moderate way, followed by the group of patients with intact incisors and the group of children who underwent traumatic history in the upper incisors, and they concluded that the combination of trauma and

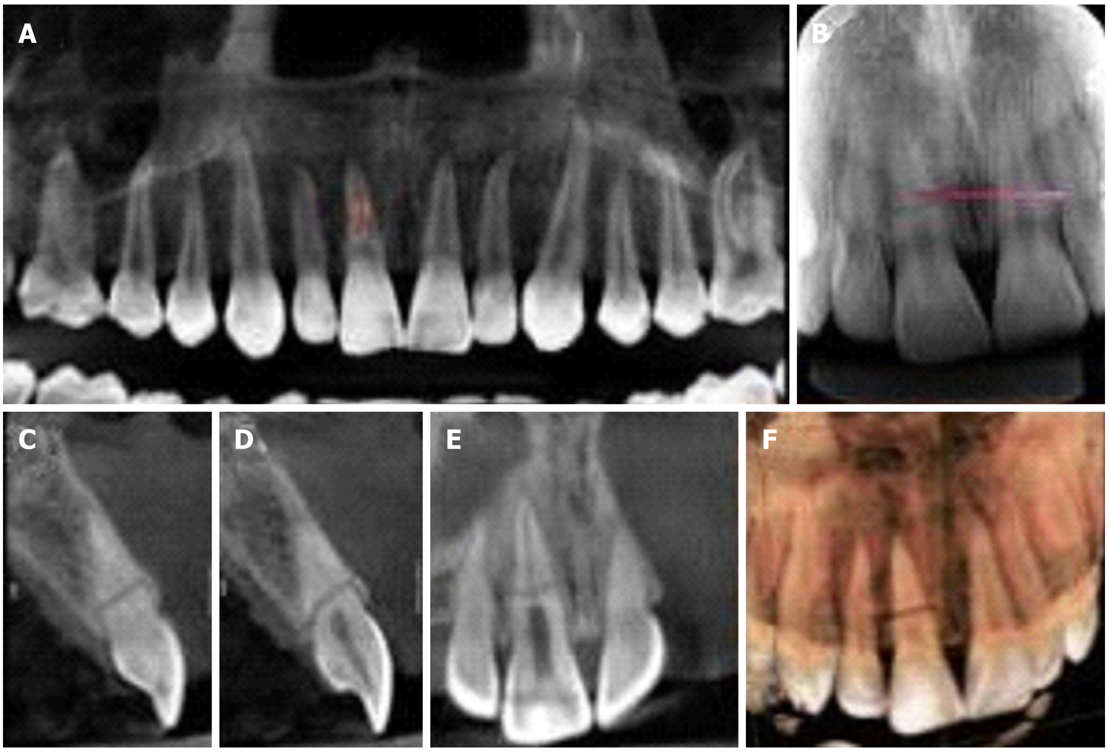

**Figure 3 Cone beam tomography.** A: Panoramic coronal reconstruction of the maxilla; B: Periapical Radiograph, showing horizontal root fracture in the middle third of tooth 11; C and D: Sagital reconstructions of tooth 11, from mesial to distal sequence; E: Coronal reconstructions of the upper incisors, from buccal to lingual direction; F: 3D reconstructions (buccal and lingual views).

**Figure 4 Digital periapical radiography.** A: Distoradial incidence; B: Ortoradial incidence. Horizontally root fractured observed in the tooth 11.

orthodontic tipping is more susceptible to complications, being the most common root resorption and loss of vitality. When roots are fractured there may be the formation of hard, connective or granulomatous tissues in the fracture line, which is related to the kind of injury[12]. As for what concerns orthodontics, it is possible to move a fractured tooth, since due care and follow ups are taken[13-15].

In order to offer the patient a better chance of healing, an appropriate plan of treatment is essential after an injury, basically because dentoalveolar traumatic outcomes must be assessed with the aid of clinical and imaginological sources[15,16].

Healey *et al*[15] presented 2 case reports concerning orthodontic movement of two teeth with root fractures, showing that it is possible to accomplish the movement but suggested a period of rest for the teeth affected because of the real possibility of increased root resorption risks. They added that such rest period is necessary for the dissipation of the stress inflicted to the periodontal ligament, in order to achieve the recovery of the inflamed tissues.

When a tooth undergoes trauma, the composing tissues may respond to it in different ways or with associations, such as those detected in the cone beam tomography of report 1, in which teeth 44 and 43 responded with partial pulp calcification; in tooth 44 it can also be observed external root resorption with apex remodeling, being possible the visualization of hypodense area suggestive of the periodontal ligament maintenance. In tooth 44, it can also be observed external root resorption with apex remodeling. Tooth 41 showed hypodense image in the periapex suggestive of apical radioluscence, while tooth 42 showed hypodense image suggestive of fracture and due to the vital response of the pulp it can be interpreted as cicatricial fibrosis. Electrical pulp test, as well as thermal tests are indicated right after an injury, and the absence of a positive result in the first weeks does not mean that a tooth needs treatment[5,7,9,17]. Therefore, our paper concludes that only clinical evaluation with visual inspection, pulp sensibility tests and periodical image assessment are able to direct the conduct and/or treatment to be taken for traumatized teeth.

## COMMENTS

### Case characteristics

A 29-year-old and a 17-year-old patients with no significant history presented horizontal root fractures detected by routine clinical examination, which went untreated, and undetected until the moment of the dental appointment.

### Clinical diagnosis

Both patients were asymptomatic and the fractures were detected by routine examinations.

### Differential diagnosis

Root perforation, periodontal disease, pulpitis.

### Imaging diagnosis

Panoramic radiograph in case one taken at the moment of the accident showed horizontal fractures in the middle third of tooth 42. Periapical radiograph at the moment of the appointment showed a thin radiolucent image and cone beam tomography showed oblique fracture with signs of healing.

### Pathological diagnosis

Horizontal root fractures.

### Related reports

Horizontal root fractures are more common in anterior teeth and may heal spontaneously or under professional intervention.

### Term explanation

Horizontal and vertical fractures are the most common traumatic dental injuries whereas crown fractures are the second most commonly reported.

### Experiences and lessons

Horizontal root fractures usually offer bad prognosis for the teeth involved; which may result in dental extractions. When the professional is aware of the fracture at the time it happened he may interfere endodontically or by splitting the teeth together to stimulate healing. This article shows that sometimes not interfering professionally may be a choice when dealing with root fractures.

### Peer-review

This is a well-structured case report.

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LETTERS TO THE EDITOR

# Commentary on: "Evaluation of variations in sinonasal region with computed tomography"

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## Abstract

This letter is a commentary on the article titled "Evaluation of variations in sinonasal region with computed tomography", published in the January 2016 issue of World Journal of Radiology. The authors definition of the secondary middle turbinate is incorrect. The authors stated that the secondary middle turbinate is an accessory turbinate that is seen between the superior and middle turbinates. It should originate from the middle meatus posterosuperior to the ethmoid infundibulum.

**Key words:** Anatomic variations; Secondary middle turbinate; Concha; Paranasal sinus; Tomography



**Core tip:** This letter is a commentary on the article titled "Evaluation of variations in sinonasal region with computed tomography," published in the January 2016 issue of World Journal of Radiology. The authors evaluated the paranasal sinus tomography of 400 patients to determine the frequency of 39 anatomic variations. Their study required a great deal of time and effort. Unfortunately, their definition of the secondary middle turbinate and the figure that showed its structure are incorrect. It should originate, however, from the middle meatus posterosuperior to the ethmoid infundibulum, not from between the middle and superior turbinates.

Çağıcı CA. Commentary on: "Evaluation of variations in sinonasal region with computed tomography". *World J Radiol* 2016; 8(12): 933-934 Available from: URL: http://www.wjgnet.com/1949-8470/full/v8/i12/933.htm DOI: http://dx.doi.org/10.4329/wjr.v8.i12.933

## TO THE EDITOR

I read the article by Dasar *et al*[1] with great interest. The authors evaluated the paranasal sinus tomography of 400 patients to determine the frequency of each of 39 possible anatomic variations. Their study required a great deal of time and effort. Unfortunately, their

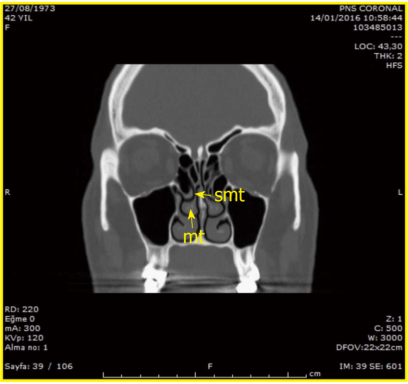


**Figure 1 Secondary middle turbinate is apparent on the right side of the figure.** smt: Secondary middle turbinate; mt: Middle turbinate.

definition of the secondary middle turbinate and the figure that showed its structure are incorrect.

The authors stated that the secondary middle turbinate is an accessory turbinate that is seen between the superior and middle turbinates[1]. It should originate, however, from the middle meatus posterosuperior to the ethmoid infundibulum, not from between the middle and superior turbinates[2]. The secondary middle turbinate is not part of the middle turbinate. The appearance of a secondary middle turbinate is probably due to the partial absence of the anterior wall of the ethmoidbulla[2].

Their figure 3D, which was used to illustrate the secondary middle turbinate, is also not appropriate. A sagittal cleft on the middle turbinate is seen in this figure, which is not an appropriate example for the secondary middle turbinate. The secondary middle turbinate is actually a bony prominence that extends from the lateral nasal wall to the middle meatus, as shown in Figure 1[2].

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