

## Radiation risks associated with serial imaging in colorectal cancer patients: Should we worry?

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### Abstract

To provide an overview of the radiation related cancer risk associated with multiple computed tomographic scans required for follow up in colorectal cancer patients. A literature search of the PubMed and Cochrane Library databases was carried out and limited to the last 10 years from December 2012. Inclusion criteria were studies where computed tomographic scans or radiation from other medical imaging modalities were used and the risks associated with ionizing radiation reported. Thirty-six studies were included for appraisal with no randomized controlled trials. Thirty-four of the thirty-six studies showed a positive association between medical imaging radiation and increased risk of cancer. The radiation dose absorbed and cancer risk was greater in children and young adults than in older patients. Most studies included in the review used a linear, no-threshold model to calculate cancer risks and this may not be applicable at low radiation doses. Many studies are retrospective and ensuring complete follow up on thousands of patients is difficult. There was a minor increased risk of cancer from ionizing radiation in medical imaging studies. The radiation risks of low dose exposure (< 50 milli-Sieverts) are uncertain. A clinically justified scan in the context of colorectal cancer is likely to provide more benefits than harm but current guide-

lines for patient follow up will need to be revised to accommodate a more aggressive approach to treating metastatic disease.

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**Key words:** Colorectal cancer; Follow up; Surveillance; Radiology; Radiation

**Core tip:** Computed tomography (CT) scans are increasingly used in the followup of patients with colorectal cancer. As multimodality treatments have become more successful in treating patients with metastatic disease follow up regimes have become more intensive. However current published treatment guidelines do not give a clear indication of the optimal frequency of follow up imaging. This review summarises the adverse effects associated with frequent use of CT scans in patient follow up.

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### INTRODUCTION

Colorectal cancer is a common cancer worldwide with one million new cases diagnosed annually<sup>[1]</sup>. Patients presenting with a confirmed diagnosis of colorectal carcinoma are first clinically and radiologically staged before multidisciplinary management encompassing surgical resection, systemic therapy and radiation is instituted.

Over the last 15 years, the management algorithm for colorectal carcinoma has become more complex as more options have become available to treat patients with both

primary and metastatic disease<sup>[2]</sup>. Consequently, more patients are now being followed more intensively after their initial diagnosis than in the past in order to detect metastatic disease and to institute appropriate treatment strategies. In most cases, follow up is based on clinical examination, regular determination of plasma carcinoembryonic antigen levels and serial imaging, usually with computed tomography (CT).

A number of recent guidelines for follow up recommend an annual CT scans of the chest, abdomen and pelvis for at least three years after initial treatment and in some cases longer (Table 1)<sup>[3-11]</sup>. However, in many institutions, follow up protocols are more comprehensive with 6 mo CT scans for the first two years after treatment when the risk of recurrence is highest and then annual scans until five years are reached. For the increasing number of patients reaching five years of follow up, the dilemma remains regarding the most optimal form of surveillance. Many authorities recommend discharge at this point but the risk of recurrent disease remains and this option is often not palatable for patients, especially for younger patients. Consequently, many continue with annual or biannual follow up and imaging.

Thus, in a patient surviving ten years after a diagnosis of colorectal cancer, there is the potential for them to undergo up to 13 CT scans of the chest, abdomen and pelvis (one scan at diagnosis, four scans in the first two years and annual scans from years three to ten). Since the average radiation dose for a chest CT chest, abdomen and pelvis with intravenous contrast is approximately 27 millisievert (mSv), where 1 mSv is equal to the dose produced by exposure to 1 milligray (mGy), this equates to a potential dose of 270 mSv over 10 years or over 100 times the average background radiation dose of 2.4 mSv per year<sup>[12]</sup>. This number can further increase if recurrent disease is detected and a further episode of staging and treatment instituted.

However, there are potential risks associated with our reliance on serial CT scans for patient surveillance. The delivered dose of ionizing radiation is associated with an increased risk of adverse health outcomes, particularly, a greater risk of carcinogenesis<sup>[13]</sup>. This concern is elevated in the paediatric population, who are more radiosensitive than their adult counterparts<sup>[13]</sup>. The aim of this investigation was to review the evidence for the risk of carcinogenesis associated with serial CT scans and, using this, to comment on currently recommended follow up regimens for colorectal cancer patients.

## SEARCH STRATEGY

A literature review was carried out using PubMed and Cochrane Library databases using the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines<sup>[14]</sup>. The keywords “ionizing radiation”, radiation induced neoplasms” and “CT” were used in PubMed [“Case-Control Studies” (Mesh) and “Radiation, Ionizing” (Mesh) or “Tomography, X-Ray Computed”

(Mesh) and “Neoplasms, Radiation-Induced” (Mesh) and “humans” (MeSH Terms) and English (lang) and “loatrfull text” (sb) and “2002/12/13” (PDat): “2012/12/09” (PDat) and “humans” (MeSH Terms) and English (lang)]. The search was limited to studies carried out in the previous 10 years, written in English, involving human subjects only and where the full text could be retrieved. The search was restricted to papers published within the last 10 years since this period includes the introduction of rapid phase spiral CT scanning and a more aggressive approach to the management of metastatic colorectal cancer. The last search was carried out on December 9<sup>th</sup>, 2012. The Board of Radiation Effects Research (BEIR VII) report<sup>[15]</sup> was also reviewed.

The eligible criteria included studies where CT scans or other ionizing radiation derived from medical imaging were used and the risks associated with the ionizing radiation were reported. Dose estimations derived from simulations such as those through the use of Monte Carlo simulation software and the IMPACT CT Patient Dosimetry calculator were included - they have been validated and used in several research articles<sup>[16-19]</sup>.

Publications of reviews, letters or case reports, studies which had no data on risk assessment and participants receiving occupational radiation exposure were excluded. Studies were initially screened on title and abstract according to the inclusion criteria above. The papers were independently reviewed by both investigators. The full text of these articles were retrieved and further evaluated. The principal summary measures included relative risk and lifetime attributable risk (LAR) of cancer. Quality assessment was carried out according to guidelines set out by Fowkes *et al*<sup>[20]</sup>.

## RESULTS

The search of PubMed and Cochrane Library yielded 344 citations. Of these, 302 studies were excluded in the initial screen of title and abstract according to the inclusion/exclusion criteria set above (Figure 1). The full text of 42 studies were assessed for eligibility. Six studies were excluded as per inclusion/exclusion criteria above. A total of 36 studies<sup>[19,21-56]</sup> and the BEIR VII report<sup>[15]</sup> were included for review. There were no randomized controlled trials. The characteristics of the studies included for review are shown in Table 2.

### Radiation associated cancer risk

Thirty-four of the thirty six studies included for review showed a positive association between ionizing radiation from medical imaging and increased risk of cancer<sup>[19,21-27,29-51,53-56]</sup>.

A recent direct study of CT scan use and cancer risk by Pearce *et al*<sup>[21]</sup> showed a leukaemia relative risk of 3.18 (95%CI: 1.46-6.94) for children and young adults who received a cumulative dose of > 30 mGy and a brain tumour relative risk of 2.82 (95%CI: 1.33-6.03) for children and young adults who received a cumulative dose of 50-74 mGy. This corresponded to an estimated absolute

**Table 1 Summary of follow up recommendations including imaging for patients with colorectal cancer**

| Ref.                                     | History and physical   | CEA                               | Abdominal imaging  | Pelvic CT                                  | Chest imaging  | Colonoscopy   | Sigmoidoscopy   |
|--|--|-----------------------------------|--|--|--|---|---|
| NCCN 2010 <sup>[3]</sup>                 | Q3-6m for 2 yr then Q6m for 3 yr                                 | Q3-6m for 2 yr then Q6m for 3 yr  | CT annual 3-5 yr   | Annually 3-5 yr for rectal cancer patients | CT annually 3-5 yr   | 1 yr then as clinically indicated                                 |   |
| PEBC 2010 <sup>[4]</sup> Stage II b-III  | Q6m for 3 yr then annual for 2 yr                                | Q6m for 3 yr then annual for 2 yr | US Q6m for 3 yr then annual for 2 yr   |  | CXR Q6m for 3 yr then annual for 5 yr                          | Yearly as long as polyps are found. If no polyps repeat 3-5 yr    |   |
| ESMO 2010 <sup>[5]</sup>                 | Colon Q3-6m for 3 yr then Q6-12m for 2 yr<br>Rectal Q6m for 2 yr |                                   | Colon CT or contrast enhanced US Q6-12m for 3 yr<br>Rectal CT 1 and 3 yr<br>CT within 2 yr |  | Colon CT Q6-12m for 3 yr<br>Rectal CT 1 and 3 yr after surgery | Colon Q1 yr then Q3-5 yr<br>Rectal Q5 yr                          | Rectal Q3-6m for 1 yr then Q6-12m                                     |
| BSG/ACGBI 2010 <sup>[6]</sup>            |  |                                   |  |  |  | 5 yr after surgery then 5 yr intervals 12m, then at 3 yr and 5 yr |   |
| ACS 2006 <sup>[7]</sup> Stage II or III  |  |                                   |  |  |  |   |   |
| ASCO 2005 <sup>[8]</sup> Stage II or III | Q3-6m for 3 yr then at physicians discretion                     | Q3m for at least 3 yr             | CT annual for 3 yr   | Consider for rectal cancer patients        | CT annual for 3 yr<br>CXR not recommended                      | At 3 yr, if normal then Q5 yr                                     | Q6m for rectal cancer patients who have not received pelvic radiation |
| Australia NHMRC 2005 <sup>[9]</sup>      | Q3-6m for 2 yr then Q6-12m thereafter                            | Q3-6m with clinical review        | CT recommended<br>No schedule  | CT recommended<br>No schedule              | CT recommended<br>No schedule                                  | Q3-5 yr initially then Q3-5 yr                                    | Rectal Q3-6m then Q6-12m  |
| ASCRS/SPTF 2004 <sup>[10]</sup>          | Q4m for 2 yr   | Q4m for 2 yr                      | Not recommended  |  | CXR: insufficient evidence                                     | 3 yr after surgery then Q3 yr                                     |   |
| NZGG 2011 <sup>[11]</sup>                | Q6m for 2 yr then yearly to 5 yr                                 |                                   |  |  |  | 3-5 yr after surgery then Q3-5 yr                                 | Rectal Q6m for 2 yr then yearly to 5 yr                               |

CEA: Carcinoembryonic antigen; CT: Computed tomography.

risk of about 1 excess leukaemia case and one excess brain tumour case for every 10000 patients who undergo one head CT scan before the age of 10<sup>[21]</sup>.

Another large retrospective study in the United States<sup>[23]</sup> reported a modest increase in cancer risk secondary to low dose (50-100 mSv) and high dose (> 100 mSv) radiation from CT scans in the elderly. In this study, an estimated 1659 (0.03%) and 2185 (0.04%) cancers were related to ionizing radiation from two cohort populations of over five million patients each<sup>[23]</sup>. Berrington de González *et al*<sup>[31]</sup> reported that an extra 29000 (95%UL 15000-45000) cancer cases could be attributable to the 57 million CT scans performed in the United States during 2007. Nearly 30% of the scans were estimated to be performed in patients aged 35-54 years, 13% in those aged 18-34 years and 7% in persons aged 18 or less<sup>[41]</sup>. The projected risks in females were higher for scans that exposed the chest due to the additional risk of breast cancer and higher lung cancer coefficients<sup>[41]</sup>.

Two studies, Blettner *et al*<sup>[52]</sup> and van Walraven *et al*<sup>[28]</sup> reported no statistically significant increased risk of brain tumours and secondary abdomino-pelvic malignancies following medical ionizing radiation respectively. Patients in the van Walraven *et al*<sup>[28]</sup> study were assessed for sec-

ondary abdomino-pelvic malignancies associated with abdomino-pelvic CT scans use in the follow up of previous testicular cancer. Patients received a median radiation dose of 110 mSv (IQR 44-190) from medical radiation imaging at 5 years follow up, a dose which was associated with increased risk of cancer in other studies included for review<sup>[22-26,31,33,35,38,41,46]</sup>.

A study of 18-35 years old participants by Zondervan *et al*<sup>[27]</sup> suggested that the majority of CT-induced cancers were from sporadic rather than frequent scanning. Whilst frequent scanning is associated with a significant cancer risk, it is usually reserved for the very ill, a population where a large proportion die before any radiation induced cancer may factor into their health<sup>[27]</sup>.

### Cancer risk in the paediatric population

Several studies assessed the risk of radiation exposure in children and young adults<sup>[21,24,27,29,32,41,42,44,49,51]</sup>. An Israeli study by Chodick *et al*<sup>[49]</sup> reported an absorbed brain dose (from a head CT) of 130 mGy for children aged < 3 years old to 30 mGy at age 16-18 years and a stomach dose (from an abdominal CT) of 51 mGy at age < 3-24 years mGy at age 16-18 years. Increasing age was associated with a reduction in cancer risk with the highest ex-

**Table 2** Characteristics of studies included for qualitative analysis

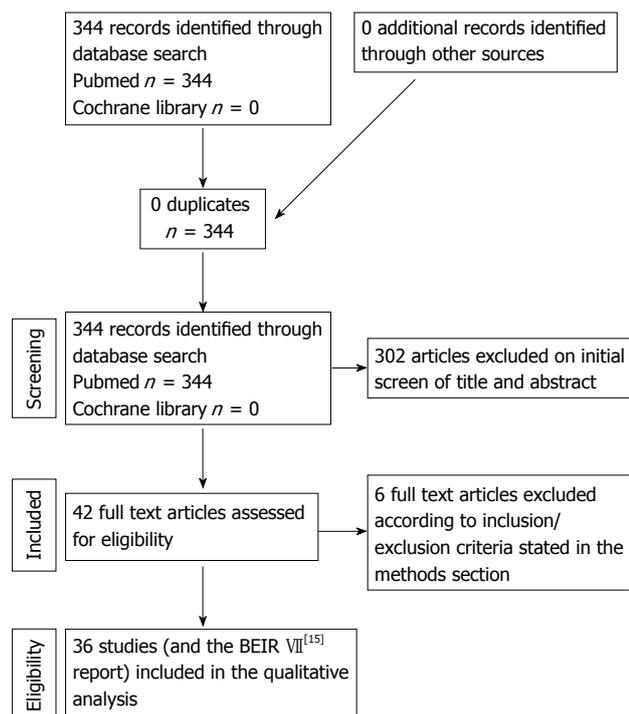
| Ref.  | Study year | Country        | Study size  | Intervention   | Study type         |
|---|------------|----------------|---|--|--------------------|
| BEIR VII report <sup>[15]</sup>                     | 2006       | United States  | Comprehensive review of all relevant biological, physical and epidemiological radiation data            |  |                    |
| Pearce <i>et al</i> <sup>[21]</sup>                 | 2012       | United Kingdom | 178604 for leukaemia and 176587 for brain tumour analysis respectively                                  | CT scan  | Retrospective      |
| Woo <i>et al</i> <sup>[22]</sup>                    | 2012       | Canada         | 1424  | Pulmonary CT angiography   | Retrospective      |
| Meer <i>et al</i> <sup>[23]</sup>                   | 2012       | United States  | Two 4-yr cohorts of 5267230 and 5555345   | CT scan  | Retrospective      |
| Muchow <i>et al</i> <sup>[24]</sup>                 | 2012       | United States  | 617   | Cervical spine multidirectional CT   | Retrospective      |
| Huda <i>et al</i> <sup>[25]</sup>                   | 2012       | United States  |   | CT scan simulation   |                    |
| Perisinakis <i>et al</i> <sup>[26]</sup>            | 2012       | Greece         |   | Triple-rule-out 256-slice CT angiography simulation  |                    |
| Zondervan <i>et al</i> <sup>[27]</sup>              | 2012       | United States  | 25104   | Chest and abdomino-pelvic CT scan  | Retrospective      |
| van Walraven <i>et al</i> <sup>[28]</sup>           | 2011       | Canada         | 2569  | Abdomino-pelvic CT scan  | Retrospective      |
| Kuhns <i>et al</i> <sup>[29]</sup>                  | 2011       | United States  |   | CT scan simulation   |                    |
| Davis <i>et al</i> <sup>[30]</sup>                  | 2011       | United States  | 205 cases, 333 controls   | Survey asking ionizing radiation exposure  | Case-control       |
| Berrington de González <i>et al</i> <sup>[31]</sup> | 2011       | United States  |   | CT colonography simulation   |                    |
| Li <i>et al</i> <sup>[32]</sup>                     | 2011       | United States  |   | CT scan simulation   |                    |
| Huda <i>et al</i> <sup>[33]</sup>                   | 2011       | United States  |   | Cardiac CT angiography simulation  |                    |
| Adams <i>et al</i> <sup>[34]</sup>                  | 2010       | United States  | 7490  | Chest radiotherapy   | Prospective cohort |
| Noor <i>et al</i> <sup>[35]</sup>                   | 2011       | United Kingdom | 202   | Plain X-ray, CT scan, nuclear medicine procedures, cardiac procedures  | Retrospective      |
| Perisinakis <i>et al</i> <sup>[19]</sup>            | 2010       | Greece         |   | Coronary CT angiography simulation   |                    |
| Falettra <i>et al</i> <sup>[36]</sup>               | 2010       | Switzerland    | 729   | 64-slice coronary CT angiography   | Prospective        |
| Feng <i>et al</i> <sup>[37]</sup>                   | 2010       | China          |   | CT scan simulation   |                    |
| Richards <i>et al</i> <sup>[38]</sup>               | 2010       | United Kingdom |   | Spine CT simulation  |                    |
| Kim <i>et al</i> <sup>[39]</sup>                    | 2010       | United States  |   | Cone beam CT simulation in a paediatric population   |                    |
| Smith-Bindman <i>et al</i> <sup>[40]</sup>          | 2009       | United States  | 1119  | CT scan  | Retrospective      |
| Berrington de González <i>et al</i> <sup>[41]</sup> | 2009       | United States  | 57 million CT scans   | CT scan  | Retrospective      |
| Raelson <i>et al</i> <sup>[42]</sup>                | 2009       | United States  | 68  | Neuroangiography   | Retrospective      |
| Kim <i>et al</i> <sup>[43]</sup>                    | 2009       | United States  |   | Multi-detector CT scan simulation  |                    |
| King <i>et al</i> <sup>[44]</sup>                   | 2009       | United States  | Two cohorts of 240 participants respectively  | CT scan  | Retrospective      |
| Sodickson <i>et al</i> <sup>[45]</sup>              | 2009       | United States  | 31462   | CT scan  | Retrospective      |
| Griffey <i>et al</i> <sup>[46]</sup>                | 2009       | United States  | 130   | CT scan  | Retrospective      |
| Huang <i>et al</i> <sup>[47]</sup>                  | 2009       | Hong Kong      |   | Fluorine 18-fluorodeoxyglucose PET/CT scan simulation  |                    |
| Einstein <i>et al</i> <sup>[48]</sup>               | 2008       | United States  |   | 16-slice CT coronary angiography simulation  |                    |
| Chodick <i>et al</i> <sup>[49]</sup>                | 2007       | Israel         | 17686 CT scans  | CT scan  | Retrospective      |
| Beyan <i>et al</i> <sup>[50]</sup>                  | 2007       | Turkey         | 15  | Radiologic imaging studies in diagnosis and follow-up of Hodgkin's lymphoma  | Retrospective      |
| Berrington de González <i>et al</i> <sup>[51]</sup> | 2007       | United States  |   | CT scan simulation   |                    |
| Blettner <i>et al</i> <sup>[52]</sup>               | 2007       | Germany        | Glioma and meningioma-747 cases, 1535 controls. Acoustic neuroma-97 cases, 202 controls                 | Interviews collecting data on diagnostic X-ray examinations, radiotherapy, CT scans, scintigrams and angiographies | Case-control       |
| Einstein <i>et al</i> <sup>[53]</sup>               | 2007       | United States  |   | 64-slice CT coronary angiography simulation  |                    |
| de Jong <i>et al</i> <sup>[54]</sup>                | 2006       | Netherlands    |   | CT scan simulation   |                    |
| Brenner <i>et al</i> <sup>[55]</sup>                | 2004       | United States  |   | CT scan simulation   |                    |
| Berrington de González <i>et al</i> <sup>[56]</sup> | 2004       | United Kingdom | Frequency of X-ray exposure estimated using worldwide survey of medical radiation use between 1991-1996 | Diagnostic X-rays  | Retrospective      |

CT: Computed tomography.

cess risk of 0.52% estimated for children aged < 3 years and 0.21% at age 16-18 years<sup>[49]</sup>. Berrington de González *et al*<sup>[41]</sup> estimated a mean lifetime cancer risk of 1 for every 1000 head CT scans at age 3 years and 1 year every 2000 head CT scans at age 15. For abdomino-pelvic CT scans, a lifetime cancer risk of 1 for every 500 scans was predicted at ages 3 and 15 and 1 every 1000 scans at age 30<sup>[41]</sup>.

### Medical imaging uses for screening

CT colonography is regarded as sensitive as optical colonoscopy and is sometimes used to detect large adenocarcinomas of the colon<sup>[57]</sup>. A CT colonography screening study estimated, using standard protocols, that patients would receive a dose of 8 mSv and 7 mSv for women and men respectively<sup>[51]</sup>. Assuming a CT colonography screen every 5 years from the age of 50-80 years, 150



**Figure 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram summary of study selection process.**

radiation-related cancers resulted for every 100000 patients screened (95% CT uncertainty interval, 80-280)<sup>[31]</sup>. The number of colorectal cancers prevented from CT colonography, based on three microsimulation models, varied between 3580 to 5190 cases per 100000 patients screened, resulting in a benefit-risk ratio of 24:1 (95% CT uncertainty interval, 13:1-45:1) to 35:1 (95% CT uncertainty interval, 19:1-65:1)<sup>[31]</sup>. The benefit-risk ratio was higher for patients aged 65-80 relative to those aged 50-64<sup>[31]</sup>.

A retrospective cohort study of 1424 patients by Woo *et al.*<sup>[22]</sup> also showed a positive benefit-risk ratio when examining the mortality benefit from preventing a pulmonary embolism *vs* mortality risk from radiation induced cancer (benefit-risk ratio of 25 for patients in the emergency department or outpatient setting and 187 for inpatients).

Brenner *et al.*<sup>[55]</sup> investigated the effects of full-body CT examinations which have become more popular in private independent radiology clinics. This study showed a single full-body CT scan in a 45-year-old adult would result in an estimated lifetime attributable cancer mortality risk of around 0.08% with 95% credibility limits being a factor of 3.2 in either direction<sup>[55]</sup>. An annual examination up till age 75 (30 examinations in total) was reported to increase the lifetime risk to 1.9% with 95% CT credibility limits being a factor of 2 in either direction<sup>[55]</sup>.

### Summary of evidence

The main objectives of this review was to provide an overview of the radiation risks involved with medical imaging and use this as a framework to better understand

risks associated with the use of CT scans for surveillance in patients diagnosed with colorectal cancer.

The majority of studies included for review showed a positive association between ionizing radiation from medical imaging and increased cancer risk<sup>[21-27,29-51,53-56]</sup>. As with all medical procedures the dilemma lies in balancing the potential harm *vs* the benefit medical imaging provides. Meer *et al.*<sup>[23]</sup> suggested that despite using conservative estimates and worst-case scenario methodology, the cancer risk was low in the elderly United States population even in patients who received dosages over 100 mSv. Whilst the risks are apparent, they need to be taken in context and two studies<sup>[22,31]</sup>, which assessed the use of CT scans to detect potentially life-threatening illnesses (colorectal cancer and pulmonary embolism), showed a clear positive benefit-risk ratio. Instances in which medical imaging may not be justified include the use of full-body CT examination as a “screening” tool, where there is potential radiation associated cancer risk<sup>[55]</sup> but poor evidence regarding its effectiveness and life-prolonging benefits<sup>[58-60]</sup>. A typical dose from a single full-body CT scan was estimated to be 16, 14 and 10 mGy to the lung, GI tract and bone marrow respectively but subject to variability due to differences in CT scanners and protocols<sup>[55]</sup>. This equates to an effective dose (weighted average dose to all organs) of around 12 mSv and an excess lifetime cancer mortality risk of 1.9% if 30 such scans were undertaken over a lifetime<sup>[55]</sup>.

In children and young adults, an age dependent cancer risk was reported, with the risk decreasing as the patients became older, particularly for head CT scans<sup>[41-49]</sup>. A recent direct study investigating CT scan use and cancer risk in patients less than 22-year-old also showed a leukaemia and brain tumour risk approximately three times higher when receiving a cumulative dose of > 30 mGy and 50-74 mGy respectively<sup>[21]</sup>. This approximates to 5-10 and 2-3 head CT scans in children < 15 years for the corresponding leukaemia and brain tumour risks stated above, respectively<sup>[21]</sup>. Children are considered more radiosensitive to the oncogenic effects<sup>[61-74]</sup>, may have a longer lifetime risk to develop cancer (particularly sarcoma, lymphoma and breast carcinoma)<sup>[49]</sup> and receive higher doses relative to adults due to their smaller body size and relative attenuation<sup>[75]</sup>.

Two studies<sup>[28,52]</sup> did not show a statistically significant association between medical imaging radiation and increased cancer risk. There could be several explanations for this. The results may be of face-value and there may be no association between medical imaging radiation and brain tumours<sup>[52]</sup> or secondary abdomino-pelvic malignancies<sup>[28]</sup>. Self-reported information and recall bias may under or overestimate radiation dose received in the study carried out by Blettner *et al.*<sup>[52]</sup>. The number of diagnostic procedures is also a crude estimate of actual radiation exposure due to the variability in radiation dose, even for the same procedure<sup>[40,52]</sup>. Van Walraven *et al.*<sup>[28]</sup> suggested that the relationship between radiation and cancer risk may not be linear, rather requiring a particular threshold

rate at which cellular repair mechanisms are overwhelmed and start carcinogenesis<sup>[76-85]</sup>.

### Limitations

Most studies included in the review used a linear, no-threshold (LNT) model as proposed in the BEIR VII report<sup>[15]</sup> to calculate cancer risks. The LNT model is based on atomic bomb survivors in the Japanese population (the Life Span study) and proposes that any radiation dose increases the risk of developing cancer<sup>[15,21]</sup>. Therefore, it is perhaps unsurprising that a majority of studies included in the review showed a positive association between medical imaging radiation and increased cancer risk.

The LNT model is not full proof, particularly with regard to application of data to non-Japanese populations and at low doses (< 50 mSv) of radiation where there is no convincing epidemiological evidence of a linear model<sup>[86]</sup>. The LNT model is still debated and a review by Pauwels and Bourguignon discusses these issues in detail<sup>[86]</sup>.

Another limitation may involve the retrospective nature of many studies and a number of authors have commented on the practicality of following up hundreds of thousands patients for their entire lifetime<sup>[31,43]</sup>. These difficulties have also been noted in another study<sup>[87]</sup>. As described above, recall bias and under or overestimation of radiation dose received may also be another limitation in case-control studies<sup>[30,52]</sup>.

With regard to the review itself, failure to identify relevant studies in the literature may have resulted in bias<sup>[14,88]</sup>. Limits were set to search for English language articles in the last 10 years only. In addition, omission of studies where the full-text could not be retrieved may have contributed to the bias<sup>[14,88,89]</sup>. As studies were not selected in an independent blinded manner, there could also have been some unjustified exclusion of eligible studies<sup>[14,88,89]</sup>.

### Implications for patient follow up

On the basis of the available literature, there is a small, but increased risk of cancer from medical radiation imaging with the risk increasing in the younger population. Many studies calculated risk using risk projection models mainly derived from atomic bomb survivors in Japan and there is a debate about the applicability of such models in low dose radiation exposure<sup>[21,90-93]</sup>. The only cohort study to date which directly assessed the risk of cancer and CT scans reported risk estimates which were broadly consistent with data from the atomic bomb survivors in the paediatric population<sup>[21]</sup>. Whether these data can be applied in the adult population is still unknown<sup>[21]</sup>.

For patients with colorectal cancer who have undergone curative resection, the current guidelines are variable with ASCO<sup>[7,8]</sup> NCCN<sup>[3]</sup> and ESMO<sup>[5]</sup> guidelines recommending annual CT scans for at least three years following diagnosis and initial treatment. However, all of the published guidelines underestimate the frequency of imaging currently employed in many cancer centres since it is now recognised that resection of localized, recurrent

disease in either liver, lung or peritoneum can be associated with long term disease control or cure<sup>[2]</sup>. The outcomes are also improved with long disease free interval from primary diagnosis making the case for ongoing follow up, even when the patients have reached 5 years post treatment.

Using data from the study of Berrington de González *et al*<sup>[41]</sup> a crude estimate of 0.013 and 0.015 lifetime excess cancers was determined for 10 CT scans to the chest, abdomen and pelvis in a 50-year-old male and female respectively. In the New Zealand context, this would equate to 39.6 excess cancers if the 1463 males and 1374 females in the 2009 New Zealand colorectal cancer registry received a conservative measure of 10 CT scans each, in the context of 1244 colorectal cancer deaths<sup>[94]</sup>. While these numbers are low and primarily include elderly patients in whom the adverse effects of radiation are reduced, ten percent of patients presenting with colorectal carcinoma are under the age of 40 years and in these patients, therapy is often most intensive and as results improve, prolonged follow up will be routine with an aggressive approach taken to treat metastatic disease. Eventually, this will require that guidelines for post-treatment surveillance address the need for more intensive surveillance strategies and make comment on extending surveillance beyond 5 years.

It may be possible to utilize non-radiation methods including magnetic resonance imaging to assess the abdomen and pelvis and contrast enhanced ultrasound for the liver although currently CT of the chest remains the gold standard for detecting pulmonary disease. A study by Schmidt *et al*<sup>[95]</sup> comparing the use whole body MRI in the follow up of 24 patients with colorectal cancer showed MRI was less sensitive (sensitivity 63%) at detecting lymph node metastases relative to FDG-PET-CT (sensitivity 93%) and had a similar sensitivity for detecting organ metastases (sensitivity 80% and 78% for PET-CT and MRI respectively). Despite the great soft-tissue resolution MRI provides for detection of pelvic recurrences of colorectal cancer<sup>[96-100]</sup>, its use for routine surveillance of the pelvis after curative surgery was “not justified”<sup>[101]</sup> on the basis that there were no differences in detection of possible cases suitable for surgical resection compared to conventional follow up protocols, rather suggesting MRI be selectively used for imaging patients following clinical, biochemical or colonoscopic assessment. The other possibility is to restrict intensive follow up to patients with adverse prognostic factors and higher risk of recurrence. However recent evidence suggests that after 3 years of survival conventional clinicopathologic factors have limited ability to predict long-term survival<sup>[102]</sup>.

Whilst nothing can be definitively concluded from the crude approximations above, clinicians should be aware of the possible risks associated with ionizing radiation when imaging patients with colorectal cancer. As with any medical intervention, the clinician needs to balance the risks and benefits, particularly more so in the younger population due to the increased radiosensitivity in this

group<sup>[61-74]</sup>. A clinically justified CT scan in the context of colorectal cancer is likely to be of benefit due to the fatal nature of the disease. Further studies of medical imaging risks in the adult population, based on empirical data using direct studies, and epidemiological data of radiation risks at low doses, would be beneficial in assessing the potential benefits and risks associated with multiple imaging in colorectal cancer patients.

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