STUDENT NAME: Victoria Chau

PROJECT TITLE:
Comparison of simulation and direct measurement methods for determining neonatal radiographic organ doses

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SUMMARY:

Patients in the neonatal intensive care unit receive numerous radiographic examinations for both diagnostic and follow up purposes such as pneumonias, respiratory distress syndrome, meconium aspirate, and cardiac anomalies, to name a few. There is concern with radiation-induced cancer development especially in pediatric patients due to smaller size, higher rate of mitotic cell division, and longer life expectancy. Although radiation dose from a single x-ray radiograph is low, we need to consider the effects of cumulative examinations. Organ doses cannot be measured directly in patients, but can be estimated using computer simulations or laboratory measurements. One commonly used computational method is the PCXMC 2.0 software, which uses Monte Carlo simulations of photon propagation in tissue to calculate an estimated dose. The doses calculated by this program have been compared with doses measured using physical phantoms and doses measured on the surface of patients. This research project will compare the PCXMC 2.0 organ doses with organ doses measured from the ATOM 703-D phantom as well as organ doses measured from pediatric cadavers, a method yet to be found in the literature. The student will use thermoluminescence dosimeters (TLDs) to measure the organ doses. The objectives for the student would be to learn radiological physics as well as experimental techniques, have clinical exposure, participate in an interdisciplinary team, learn to use the software program PCXMC 2.0, TLDs, and x-ray machines to calculate and measure doses, and to recognize and appreciate patient safety in the field of pediatric radiology.

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1. Introduction

Since the introduction of medical radiology in the beginning of the 19th century, ionizing radiation has changed the practice of medicine. With constant evolution of technologies and imaging techniques, patient diagnosis and care has improved, especially with the advent of digital radiography and computed tomography (CT). X-ray imaging is used in all different avenues of practice from trauma cases to surgical cases, from skeletal injuries to respiratory, cardiac or gastric complications; x-ray imaging is used commonly in every day practice in medicine for both diagnostic purposes as well as therapeutic purposes.

However, there exists concern for consequences of exposure to ionizing radiation especially for those undergoing frequent medical imaging procedures. The largest concern involves radiation-induced cancers [1-3]. Only recently has there been data supporting radiation-induced cancers with studies following the Japanese Atomic bomb survivors over the last approximately 60 years. These studies have shown an excess incidence of leukemia and a wide range of solid cancers (lung, thyroid, colon, breast and digestive organs). These studies allow for extrapolation of risk estimates to low doses of medical irradiation using the variety of doses the Atomic bomb survivors were exposed to. The doses the survivors were exposed to ranged from 0 to 4 Gy [1-3]. For example, it is estimated linearly that solid cancer rates are increased by 5% by a dose of 0.10 Sv, a dose equivalent to 1000 chest x-rays [4]. Furthermore, these studies have also shown that children are more radiosensitive to radiation than adults [1-3].

When x-rays are absorbed by cells in the body, there can either by DNA strand breakage directly or indirectly from the production of free radicals from high energy photons. If the breaks occur in such a way that both strands of the DNA break, it is possible for the chromosome to have deletions or translocations, potentially giving rise to the biological effects of radiation. As previously mentioned, children are more radiosensitive. This is not only due to a longer timeline to express any of these effects but as well to an increase for these chromosomal damages to occur since the cells of children, especially infants, are at a high mitotic state. The small size of the infant also brings the organs closer together and more in the path of the direct beam [3,5,6,7].

This raises concerns in pediatric patients, especially those staying in neonatal intensive care unit (NICU) who receive multiple radiographic exams daily for both diagnostic and follow up purposes. These patients have a variety of health issues such as meconium aspiration, respiratory distress syndrome, pneumonias, any cardiac malformations, obstructed bowel, of which diagnostic radiographs are ordered regularly to follow up on progress [8]. On average, these patients are subjected to 8-10 radiographs during their stay with the potential for even more [6,8-11]. The most sensitive organ sites in pediatric patients include lung, stomach, colon, breast, gonad, esophagus, bladder, and liver [8]. These organs are often in the x-ray field for chest radiographs and abdominal radiographs, the most common diagnostic imaging in the NICU.

CT, which delivers about 100 times the radiation dose of a conventional radiograph, is not commonly used in NICU patients; therefore, it is not normally of concern for NICU patients as far as radiation risks are involved. X-ray radiographs deliver fairly low amounts of radiation to the patient, and carry a low risk of development of cancer. However, we need to be concerned with the number of radiographs patients may be exposed to and consider the effects of cumulative doses .

To quantify radiation, we use the metric International system (SI) units of gray (Gy). Dose absorbed is measured in Gy and is equal to a joule per kilogram (J/kg). Organ dose is the amount of radiation absorbed by the respective organ and is measured in Gy [12]. Dose is deposited in patients through the interactions between x-ray photons and tissue material that take place at the atomic level. These interactions cause the photon to either be completely absorbed or scattered. Both of these events generally lead to the deposition of energy in the tissue.

We can estimate doses using either representative phantoms or Monte Carlo simulations. A phantom is a model of human tissue and structure made of comparable material composition depending on the organ structure (soft tissue or bone). There are different models of phantoms available. For example, there are computational phantoms defined by mathematical expressions, a voxel phantom which is based on CT and MRI images of a patient, and physical or anthropomorphic phantoms, which is the model used in this study [13]. While the use of physical phantoms is useful for measuring doses from different imaging technologies, the use of phantoms is also labour intensive and time consuming.

PCXMC 2.0 is a Monte Carlo program that calculates patients' organ doses and effective doses in medical x-ray examinations using Monte Carlo method [13]. The Monte Carlo method uses a stochastic mathematical simulation of the histories of a photon as it interacts with matter. The program allows the user to calculate individual doses for each patient by adjusting the doses according to the height, mass, and approximate age (0, 1, 5, 10, 15, adult) of each patient. It is based on a mathematical computational hermaphrodite human phantom model of geometrical shapes as organs. Users are able to individualize each simulation by PCXMC 2.0 by inputting the height, weight, and x-ray geometries such as beam entry, air kerma, field size, and source to image distance. With this information, the program outputs organ doses, effective dose and risk estimates [13].

There have been reasonable agreements of the PCXMC 2.0 calculations with comparisons to measurements with phantom models [13]. Smans et al. also compared PCXMC 2.0 to calculated doses in two premature baby voxel phantoms with weights of 590 g and 1910 g showing PCXMC 2.0's applicability to the small sizes of neonates. However, there were differences in measurements which were explained by the differences in phantom model simulation and positioning in the x-ray field. Smans et al. used two different Monte Carlo simulations to compare the different models, the voxel phantom simulation scheme and PCXMC 2.0, with the assumption that the voxel phantom simulation was more accurate. Other studies have also shown differences with use of voxel phantoms [8,13].

There have also been studies which estimate the entrance surface doses by placing thermoluminescent dosimeters (TLDs), which are small detectors, directly on the surface of neonatal patients prior to examination to determine the entrance surface dose [14,15]. To date, this has been the method to estimate doses to patients directly; however, there are no published studies available citing methods involving in vitro measurements.

TLDs allow for direct measurement of irradiation, especially in the use of physical phantoms. They trap high energy electrons and release the electrons when heated at a high temperature which are converted into a charge reading (nC). The Harshaw TLD 100s have been noted to have good equivalency to tissue, which makes them useful to use for clinical applications on top of their small size [16].

There are few studies available that have been able to measure directly doses delivered to organs of patients. There has been a published study using cadaver mice [17] but none with human cadavers, especially to compare with PCXMC 2.0. The purpose of this study is to compare organ doses calculated using the PCXMC 2.0 Monte-Carlo software to measurements of organ doses obtained from both physical phantom measurements and pediatric cadaver measurements. We want to assess the applicability of PCXMC for use with neonates. The estimates are considered valid if there is a 5-10% agreement.

2. Materials and Methods

2.1 TLD Calibration

We used high sensitivity TLDs (TLD-100 H, Harshaw) made of Lithium Fluoride: Magnesium, Copper, Phosphor (LiF: Mg, Cu, P) for their high sensitivity and reusable nature. The size of each individual TLD was 3.1x3.1x0.9 mm thickness.

The chips were read using the Harshaw QS 3500 Reader (Harshaw, Thermo Scientific), which measures TLD response as a charge reading using the WINREMS software at a temperature of 240°C for approximately one and a half minutes. TLDs were calibrated for intra-TLD consistency. TLD chips with a calibration factor of more than one standard deviation from the average calibration factor were discarded. TLDs were handled with vacuum forceps due to their sensitivity to contact.

To acquire TLD dose readings (nC), we read the TLD prior to use, took repeated readings after the TLDs were irradiated and subtracted the pre-irradiation readings from the post-irradiation readings (See Appendix for details). To use the charge readings as a measurement of exposure (mR), we performed calibration tests to relate TLD response to exposure readings given by the Unfors Xi multi-purpose detector (Unfors, Sweden) to obtain a conversion factor (nC/mR).

2.2 Physical Phantom Measurements

We used the ATOM 703-D anthropomorphic newborn phantom (CIRS Inc, VA) to measure organ doses. This sectional physical phantom weighed 3.4 kg and had a height of 51 cm (Figure 1a). The physical phantom had pre-drilled plugs for the insertion of TLDs in regions that represented various organs (Figure 1b, c). The physical phantom had 95 dose measurement locations covering 19 organs and consisted of three different tissue-mimicking materials: lung, soft tissue and bone.

To measure organ doses, TLDs were first annealed as previously described. We used a custom-loader to insert the TLD chips into the phantom plugs of the various organs (Figure 2). There were four TLDs per plug except for the plugs for the scapula and clavicles, of which there were placements for three TLDs. The physical phantom was then reassembled and irradiated with an AP chest/abdomen technique with 60 kVp, 3 mm Al filtration and 0.5 mAs. The image distance (SID) was 69.2 cm, the field size was 25.7 cm x 18.4 cm and the incident air kerma was 40.8 μGy. The x-ray field exposed the physical phantom's organs ranging from just below the thyroid to just above the testes. These settings were similar to those used in the NICU, except for the SID, which is typically set at 100 cm in NICU. The x-ray machine we used had a fixed SID, therefore, we were unable to set the SID to that of the NICU. Organ doses were determined using the following formula:

Equation 1: $D_T = R_c K \cdot C \cdot (8.767\ \mu Gy/mR) \cdot F$

where D_T was the organ dose, C was the calibration factor (nC/mR) and F was the air to tissue dose conversion factor. We used value of F of 1.06 for soft tissue and 3.38 for bone [18]. For active bone marrow (ABM), dose was determined using weighting factors from the study by Christy [19].

The organ doses were calculated by taking the average of all the TLD readings for the respective organ. The standard deviation calculated was also calculated from all the TLD readings for the organ.

2.3 Pediatric Cadaver Measurements

To measure the inner dose in the pediatric cadavers, after annealing, the TLDs were packaged in small labelled paper envelopes sealed in small plastic sachets to prevent contamination with blood or other bodily substances that may influence the precision of the TLD measurements. Once the anterior rib cage was removed and the appropriate septic autopsy procedures were completed, we placed the packaged TLDs around the organs of interest (lungs, liver) posteriorly, anteriorly, and within lobes when possible. The number of TLDs per organ varied slightly depending on the size of the cadaver. For the left lung, two TLDs were placed posteriorly, two anteriorly, and one within the lobe if possible. For the right lung, three TLDs were placed posteriorly and anteriorly, and two were placed within the two lobes of the right lung when possible. For the liver, we used the same number of TLDs placed posteriorly as for anteriorly. Once inserted, we re-placed the rib cage onto the chest cavity and sutured the skin to close the cavity as much as possible. If there was excess pooling of blood in the chest cavity, the cavity was packed and the packing was then removed.

The TLDs were irradiated using a portable x-ray machine (AMX3) with settings at 60 kV, 4 mAs, SID of 40 inches (101.6 cm) and incident air kerma of 140 μGy for cadavers 1 and 3, 131μGy for cadaver 2 and 146.8μGy for the physical phantom. We chose to increase the dose to achieve better photon statistics. The x-ray field was collimated to be an AP chest abdomen radiograph including both arms, just above the thyroid and just below the anterior superior iliac spines. The depth between sternum and spine and x-ray field sizes were measured individually for each cadaver and for the physical phantom (Table 2).

Once irradiated, the TLDs were removed and read. We used equation 1 to calculate the dose for each TLD. All TLDs used for their respective organ were averaged to calculate the organ dose. The standard deviation was taken over all the TLDs per organ.

Consent was not required from the Bannatyne Research Ethics Board Committee since we deemed it an insensitive time to request consent and since pediatric cases routinely are examined radiographically during autopsy procedures.

We also measured the organ doses for the organs of interest (lungs, liver) with the physical phantom using the same techniques as for the cadaver to compare doses.

2.4 PCXMC 2.0 Simulations

In PCXMC 2.0, we entered the age, height, mass, exposure techniques and irradiation geometry, including the incident air kerma for each individual pediatric cadaver or physical phantom with their respective characteristics and parameters (Figure 3). The simulation was performed with $2x10^6$ photons and the statistical uncertainty was 1.33%.

For each organ common to PCXMC 2.0, the ATOM 703-D phantom, and the organs of interest from the cadaver measurements, we calculated the percent difference between the organ dose values obtained from TLD measurements and simulations using the following formula:

$$\text{Equation 2: } \Delta_T = \frac{|D_T^{TLD} - D_T^{MC}|}{D_T^{TLD}} \times 100\%$$

where the T represents the organ, D_T^{TLD} is the measurement obtained from the TLDs from either pediatric cadaver or physical phantom and D_T^{MC} is the calculated dose from PCXMC 2.0.

3. Results

3.1 Physical phantom and PCXMC 2.0 organ dose comparisons

Table 1 shows the measured and simulated organ doses with their respective percent differences between the measured organ doses with the physical phantom and the calculated organ doses by PCXMC 2.0. There were 6 of the 18 organs that agreed within the limit of 5-10%, and 10 organs of the 18 that agreed with a difference less than 20%. The organs with the largest difference magnitude were thyroid, testes, and breasts with disagreements of 86.8%, 86.9% and 69.6% respectively. The organs with the best agreement were lungs, liver and ovaries with percent differences of 1.4%, 2.6%, and 2.2%, respectively. The differences for the organs range from 1.4% for the lungs to 86.9% for the testes. The median percent difference was 15.1% and the average percent difference over the 18 organs was 28.1%.

Table 1 also shows disagreement of organ doses between PCXMC 2.0 and voxel phantoms by Smans et al. [5].

3.2 Pediatric cadaver, physical phantom and PCXMC 2.0 organ dose comparisons

Table 2 shows the measured and simulated liver and lung organ doses for the pediatric cadavers as well as the physical phantom with their respective percent differences. The organ doses are fairly similar across cadavers with a variance of 4.1% for the lungs and 1.6% for the liver. However, when compared with PCXMC 2.0, the percent differences are higher than expected with the best agreement obtained in the lung doses of cadaver 2 with 14%.

The ATOM 703-D phantom had a height and mass similar to that of cadaver 1, but had doses less than that of cadaver 1 with a difference of 18.9% for the lungs and 21.8% for the liver. When the physical phantom measurements were compared to the PCXMC 2.0 simulation for the physical phantom, the differences were not as large falling between 5-10% (Table 2).

As the weight of the cadavers increase, the doses are expected to decrease. The PCXMC 2.0 values for the organ doses follow this trend for the cadavers, but cadaver 2 has a lesser dose than cadaver 1 for the lungs. However, due to the small sample size, it is difficult to confidently comment on any trends.

4. Discussion

The organ doses have a wide variation between the doses calculated by PCXMC 2.0 and measured using the ATOM 703-D phantom. However, the organs that are more anterior and more centered within the x-ray field (lungs, liver, gall bladder, spleen, stomach) seem to have a better agreement than the organs on the outer edges of the field or are located posteriorly in the physical phantom.

In Makri's study, the organs with highest dose for a chest radiograph are the breasts, lung, bone marrow and bone surface. In a chest-abdomen radiograph, stomach, liver and skin are added to that list [8]. This is also consistent with our measurements as the breasts, lung, stomach and liver have the higher doses.

The thyroid and testes both have a disagreement of 87%. These organs are partially irradiated in a combined A/P chest-abdomen radiograph. Despite care exercised in matching the image field of view, the dose difference may be attributed to variations in identifying the irradiated field of view with the x-ray machine and matching it with PCXMC 2.0 software. Positioning is likely a factor involved.

The breasts have a disagreement of 70%. The breasts are small organs and the physical phantom has one measurement location per breast. The small size of the breasts and few TLD measurements may be contributing to the low agreement and large uncertainties.

Large dose differences between the two methods for adrenals and kidneys are also observed. These two organs are posteriorly positioned in the trunk. In the physical phantom, the anterior-posterior depth of the section with the plugs for the adrenals and kidney is 8.5 cm, with the kidney dose measured at 6.8 cm from the surface and the adrenals dose measured at 6.2 cm from the surface. This suggests low measurement agreement due to attenuation. Also, in PCXMC 2.0, each adrenal is designed as a half an ellipsoid superior to the kidney whereas in the physical phantom, the TLD plugs for both organs are in the same plane, in the same section.

Best agreement between measured and simulated organ doses occurred for the lungs and liver. In the physical phantom, the lungs extend over three sections and have a total of 15 dose measuring locations for a total of 60 TLDs. The liver, similarly, has 13 measurement locations with a total of 52 TLDs. It is possible that the relatively large volume of these organs and the large number of measurement locations distributed in the volume contributes the agreement between PCXMC 2.0 and the TLD measurements. With larger organs, differences due to exact organ location and shape are minimized and the large number of dose measurement points improves measurement statistics.

Studies have shown that there is comparable agreement between phantoms and PCXMC 2.0 [13]. The study by Smans et al. showed some disagreement with use of a voxel phantom, but this was attributed to the use of the type of phantom that was not comparable with phantoms that were used for Monte Carlo calculations and based upon assumptions that voxel phantoms are more accurate [5,13]. Our results using an anthropomorphic phantom had some variability in comparison with PCXMC 2.0 but had reasonable agreement, especially with the larger organs such as the liver and lungs. We can also observe in Table 1 there was also variability in Smans et al.'s study [5]. The median percent difference over all the organs for phantom 1 from the study

by Smans et al. [5] was 23%, and average percent difference for phantom 1 was 28.7%. For phantom 2, the median percent difference was 13.5% and the average percent difference was 18.4%. These values are comparable to the median (15.1%) and average (28.1%) percent differences of the doses for the physical phantom obtained in our study. It would be interesting to compare physical phantom measurements with a voxelized Monte Carlo simulation such as that used by Smans et al [5]. This is the subject of future work.

However, when we carried over the comparison using pediatric cadavers, our expectations were not met the same way as it did for the physical phantom. The doses are comparable when comparing doses between cadavers both with PCXMC and with our TLD measurements, which is to be expected since all the parameters were consistent; nevertheless, when comparing the doses generated by PCXMC 2.0 and the TLD measurements, there was a large difference between doses.

There was also a high standard deviation for the cadaver organ doses. This is because the standard deviation was calculated using all the TLD measurements for the respective organ despite its location posteriorly, anteriorly or within the organ lobes. The PCXMC 2.0 organ dose falls within the variation of the cadaver lung organ doses (Figure 4) but does not for the liver organ doses (Figure 5).

When we re-did the experiment procedure using the ATOM 703-D phantom (who is comparable to size of cadaver 1), we measured a lower dose than cadaver 1, and the doses between PCXMC 2.0 and TLD measurements agreed within the limit we set of 5-10%. This agreement of the liver and lungs is consistent with our initial comparisons of PCXMC 2.0 and physical phantom measurements.

The difference between the physical phantom measurement and cadaver 1 was 18.9% for the lungs and 21.8% for the liver. The dose in cadavers may have been higher than the lung dose measured in the phantom due to low inflation of the lungs. A paper on pediatric phantoms notes that ATOM phantoms tissue simulation is ideal for all organs except lungs [20].

It is also possible that the material used for the physical phantom is not comparable to human tissue, or the organization of tissues is not the same. The physical phantom is a solid structure. The organs in the physical phantom are completely surrounded by solid material. In humans, on the other hand, the organs are suspended by connective tissue with some free space surrounding them, especially in the abdominal cavity. The solid nature of the phantom may have attenuated the dose giving rise to a larger dose measured from the cadavers.

There also may be limitations to PCXMC 2.0 that contribute to such a difference. PCXMC 2.0 scales the size of its mathematical model, which is an average of a large population of sizes. It does not specifically generate a model for every individual patient. Once the mass and height have been adjusted, the software program creates a scaling factor to scale up or down the organs. All dimensions of the organs are multiplied by these scaling factors. Variability of fat is neither changeable nor accounted for, and due to scaling, the organs may also move position [13].

Another limitation that PCXMC 2.0 does not take into account is the variability in the exposure in the x-ray beam field, as it is not uniform. The x-ray machine we used for the measurements of the physical phantom had variation in the exposure depending on the axis. There was a

significant decrease in dose when measuring from the thorax, where the center of the beam is directed, to the head and a decrease from the thorax to the feet. However, there was better uniformity of measurements when measuring doses laterally from the center of the beam. To address this issue in the future, we may be able to reposition the physical phantom in the axis with the better uniformity.

There are no published studies using cadavers to measure organ doses available to compare our cadaver results to. It is difficult to say with certainty, especially with such a small sample size, if the disagreement is significant or from errors in the experimental design, as there were some limitations to our experiment. These limitations were due to the nature of the availability and amount of time of availability of the cadavers. For this reason, we were unable to repeat measurements for organ doses in each of the cadavers. Also, there is potential for TLD damage from bodily fluids which would have skewed the readings. Further investigation is needed.

Dose estimation using TLDs with an anthropomorphic physical phantom and PCXMC 2.0 simulations are advantageous in different situations. PCXMC 2.0 has a clear advantage in requiring less attention and providing faster results. Taking measurements with a physical phantom requires a large amount of time mainly due to the annealing process of the TLDs. MC-based simulations take advantage of the use of computing technology, which requires less human attention. It should be noted that PCXMC 2.0 simulation time is dependent on the photon histories simulated. As the number of photons increase, the statistical power yields more accurate doses, however consequently increasing simulation time. If more accurate results are desired, PCXMC 2.0 may also be time consuming. Another advantage PCXMC 2.0 provides is the ability to modify the mathematical phantom to the desired model. Physical phantoms have a fixed weight and height which may not represent the patient of interest. Physical phantoms are also costly.

The use of pediatric cadavers to measure organ dose had its limitations, as previously mentioned, although it would be worth further comparing organ doses achieved from phantoms and cadavers to investigate how similar or different the two are. Future cadaver organ projects may be more feasible either using animal models comparing doses with animal based Monte-Carlo simulation or using adult cadavers since the adult cadavers are more readily available for use and available for repeat use than pediatric cadavers. The size of the adult cadaver is larger than a pediatric cadaver; therefore, it should be more feasible to use more TLDs on the organs of interest. Since TLDs are time consuming, especially from the annealing process, other radiation measuring devices may be useable. MOSFET dosimeters may be an option as they give out immediate readout measurements [21]. Comparisons of cadaver measurements to other Monte Carlo simulations, such as the voxel phantom scheme used in study by Smans et al. may also be of interest [5].

5. Conclusions

To conclude, physical phantom-based comparison to PCXMC 2.0 is more reliable than in-vitro measurements. The uncertainty in the doses calculated by PCXMC 2.0 makes the variations more acceptable. PCXMC 2.0 allows medical professionals to quantify an estimated dose of radiation a patient is receiving without much labour or time. While it is uncertain if PCXMC 2.0 gives an individualized, exact dose, we can still use the estimated values as a guideline to assess the risks medically-related radiation has on patients as patient safety and care is a priority in

radiological practice. This is particularly important in paediatrics and neonatology since these patients often receive multiple radiographic examinations. Software programs like PCXMC 2.0 will allow us to quantify these exams, and will help the patient and the medical staff assess radiation-related risk and make appropriate decisions for the care of the patient without delivering unnecessary radiation.