Development of a radiopharmaceutical dose calculator for pediatric patients undergoing diagnostic nuclear medicine studies

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Objective: It is important to ensure that as low as reasonably achievable (ALARA) concept during the radiopharmaceutical (RPH) dose administration in pediatric patients. Several methods have been suggested over the years for the calculation of individualized RPH dose, sometimes requiring complex calculations and large variability exists for administered dose in children. The aim of the present study was to develop a software application that can calculate and store RPH dose along with patient record. Materials and Methods: We reviewed the literature to select the dose formula and used Microsoft Access (a software package) to develop this application. We used the Microsoft Excel to verify the accurate execution of the dose formula. The manual and computer time using this program required for calculating the RPH dose were compared. Results: The developed application calculates RPH dose for pediatric patients based on European Association of Nuclear Medicine dose card, weight based, body surface area based, Clark, Solomon Fried, Young and Webster’s formula. It is password protected to prevent the accidental damage and stores the complete record of patients that can be exported to Excel sheet for further analysis. It reduces the burden of calculation and saves considerable time i.e., 2 min computer time as compared with 102 min (manual calculation with the calculator for all seven formulas for 25 patients). Conclusion: The software detailed above appears to be an easy and useful method for calculation of pediatric RPH dose in routine clinical practice. This software application will help in helping the user to routinely applied ALARA principle while pediatric dose administration.

Keywords: As low as reasonably achievable, pediatric dose, radiopharmaceutical, software

INTRODUCTION

The number of nuclear medicine patient’s examinations is increasing rapidly day-by-day and so is the percentage of pediatric cases. Because of their expected longer survival and higher radio sensitivity in comparison to adults, radiation induced cancer may express in children during their life time. Since it is not possible to ascertain that the expression of cancer is only due to radiation, “linear non-threshold” model is used for setting up the radiation protection guideline. Consequently, the concept of “as low as reasonably achievable” (ALARA) is followed while dealing with radiation. In diagnostic nuclear medicine, ALARA will be in practice only when each and every patient receives the minimum amount of RPH dose that is necessary to produce a good quality diagnostic scan. As individuals can have varying degree of radio sensitivity (e.g., children have high sensitivity), along with variation in height, weight, lean body mass, body mass index, surface area and the equipment used to diagnose may also differs in sensitivity; therefore, a fixed dose of RPHs to each patient is not according to ALARA.

Appropriate selection of administered RPH activity depends on patient population, choice of equipment, specific requirement of clinical protocols and the physician’s judgment. It is also possible to still lower the administered activity.[1-2] There is a large variability in the administered RPH dose in children.[3] Several methods to calculate RPH dose for children have been suggested over the years. Most of these methods are based on scaling adult dose according to age (Young’s,[4,5] Webster’s[6] and Solomon [or Fried’s][5]), weight (Clark’s[6,8]) or body surface area (BSA); Clark’s area rule,[4,8] (Du Bois and Du Bois,[9] Mosteller,[7] Boyd,[8] Gehan and George,[8] Haycock et al.[10] and many others).
The group which uses BSA and Webster’s formula advocates that more counts were needed to obtain good quality images in infants and small children.\(^{[11]}\) Other group using weight based RPH have reported that the resulting effective dose are far lower than the current established threshold for radiation induced carcinogenesis when RPH dose are based on weight.\(^{[12]}\) The European Association of Nuclear Medicine (EANM) dosimetry and pediatrics committees introduced a dose card for major pediatric nuclear medicine diagnostic procedures, including a set of minimum activities.\(^{[11,13]}\) To overcome complexity of calculation using this approach requires software.

We intended to decide a formula from a list of formulas (used to calculate RPH dose) and use it in routine practice. Some of the formulas had multiple terms involving exponent, addition, multiplication and division of the decimal number and required dedicated manpower to devote considerable attention and time to produce an accurate result. Therefore, there was a need to develop a software application that can not only reduce the time of calculation, but also enhances the accuracy. The aim of the present study was to develop a software application that can calculate RPH dose by all the formulas mentioned above and store it along with the patient record for the further research.

**MATERIALS AND METHODS**

The development of the software application was divided into following four tasks:

a. Selection of the methods/formulas to be included.
b. Selection of the operating system and database package.
c. To make tables, form and query
d. Validation of the program.

**Selection of the methods/formulas to be included**

We reviewed all relevant literature to find out the most commonly used formulas to calculate RPH dose in the Nuclear Medicine and documented it. We included EANM dose card for the children,\(^{[14]}\) weight based BSA and Webster’s formula in the program.\(^{[4-7,9,10]}\) The Dose formulas that we have included are detailed in Table 1. To calculate BSA, we have used the following formula:

\[
BSA = \text{Weight (Kg)}^{0.425} \times \text{Height (cm)}^{0.725} \times 0.007184
\]

**Selection of the operating system and database package**

Microsoft Access is a software development tool and a database management system that combines Microsoft Jet Database Engine with a graphical user interface. It is possible to import and export data to many format such as Excel. Access stores all database tables, queries, forms, reports, macros and modules in the Access Jet Database as a single file. The programming language available in access is Microsoft Visual Basic for Applications, which is nearly identical to Visual Basic 6.0 (VB6). VBA code can be stored in modules and code behind forms and reports. Databases less than 1 GB in size (which can now fit entirely in RAM) and 50 users can access database simultaneously. We found MsAccess to be the best suitable option for our purpose. We selected window operating system (more commonly used) and Microsoft Access database application (that comes with MS-office or can be purchased as a separate package). We developed this software application using Windows 7 Home Basic Copyright © 2009 Microsoft Corporation and Microsoft Access [installed on the processor Intel® Core™ i3-2120 CPU @ 3.30 GHz, 2.0GB RAM and 64-bit operating system, on the computer (Hewlett-Packard Company)].

**Designing tables form and query**

A representative detail of the program is shown in Figure 1. In that program, Fig 1_Tables 1 and 2 were designed to store the information available in the EANM dose card so that it can be used as a lookup table. Fig 1_Table 3 was designed to store the patient record. Fig 1_Table NM was designed so that multiple study of the patient can be stored together. Figure 1 shows the list of fields available in the table NM, Tables 1-3 and their relations. NM_ID of Fig 1_Table NM is of the type one-to-many relation with patient ID of Fig 1_Table 3. RPHID of Fig 1_Table 3 has one-to-one relationship with RPHID of Fig 1_Table 1 and weight of Fig 1_Table 3 has one-to-one relation with weight ID of Fig 1_Table 2.

A data entry form with three command buttons find record (to find the record), add the record (to add new record and save the data) and increment investigation (to increment investigation number by one) was designed [Figure 2]. Visual Basic codes were written for add record and increment investigation command.

**Table 1: List and details of the formula used by the current program**

| Method                  | Formula                                      |
|-------------------------|-----------------------------------------------|
| BSA based               | (BSA [m²]/1.73 m²)×adult dose                 |
| Clark                   | (Weight [lbs]/160)×adult dose                |
| Solomon (Fried)         | (Age [month]/180)×adult dose                 |
| Young                   | (Age [year]+age [year]+12)×adult dose        |
| Weight based            | (Weight [kg]/70)×adult dose                  |
| Webster’s formula       | [(age+7)× adult dose]/(age+1)                |
| EANM pediatric dose card | Baseline activity* multiple (based on weight and radiopharmaceutical dependent factors)\(^{[12]}\) |

BSA: Body surface area, EANM: European Association of Nuclear Medicine

**Table 2: Time required for calculating radiopharmaceutical dose for 25 patients with different formula, manually and using the program**

| Formula                  | Manual time | Computer time (including data entry) |
|--------------------------|-------------|---------------------------------------|
| BSA                      | 10 min 20 s |                                       |
| Webster’s                | 26 min 11 s |                                       |
| Weight based             | 09 min 41 s |                                       |
| EANM                     | 27 min 05 s | 2 min (for all seven formulas)        |
| Young’s                  | 09 min 30 s |                                       |
| Solomon                  | 09 min 56 s |                                       |
| Clark                    | 09 min 20 s |                                       |
| Total time               | 102 min 03 s| 2 min (for all seven formulas)        |

BSA: Body surface area, EANM: European Association of Nuclear Medicine
Validation of the software application
We used Microsoft Excel spread sheet to verify the accurate execution of dose calculation. Three hundred patients data entry have been made and software has been validated for the intended application. Calculation time was noted by performing manual calculation by two medical physicists using stop watch and compared it with the time taken by this program. Complete time required to calculate the RPH dose was calculated by putting a timer on the form and it started when the user enters NMRefNo and it stops when he presses add record button, this is the data entry time. The calculation time starts when the user presses the query until the result display. Reduction in calculation time was calculated by comparing the manual time and computer time required in 25 patients.

RESULTS
The objective of the study was to develop a software application to calculate the RPH dose by all selected formulas and store the result along with the patient record. The Manual and computer calculation time for 25 patients are detailed in Table 2. Any of the formula used from 1 to 7 indicates that the time taken by computer is very less than the time taken manually.

Software application has one data entry form [Figure 1] to enter the patient details. It has two combo boxes one for selecting RPH and another for weight of the patient. Once, user selects the RPH of interest from the list of displayed RPHs, the software automatically populate the data in three different fields named as “class,” “baseline” and “minimum.” Similarly, after selection of weight the value of the field “multiple” is automatically populated. In this way the software minimizes the data entry error and also reduces the number of data entry. In fact, user needs to enter the patient name, age, sex, height and weight. The remaining four fields on the form are automatically populated. Once the data entry is complete, user can click the add record command button to save the record and then view the RPH dose by double clicking the RPH dose in MBq query [Figure 2].

By running the query “RPH dose” in MBq we can view the RPH dose of each patient in MBq based on each selected except that based on European dose card. For pediatric patients (age <18 years) RPH dose based on European dose card is available [Figure 3]. The query results can be exported to the Excel sheet for further analysis and research. We did the same calculation using Microsoft Excel and found exactly the same results as with Microsoft Access. User can backup data by using standard backup facility of Microsoft Access. The written Visual Basic code is password protected to prevent accidental damage.

DISCUSSION
To implement ALARA in routine practice, RPH dose needs to be tailored according to each individual patient, especially in children.
We have developed a software application to calculate RPH dose based on weight, BSA, Webster’s formula and EANM dose card. It is robust and user friendly. It automatically generates nuclear medicine reference number for each new patient and a scan ID for each new investigation. Only name of the patient, age, sex, height (in cm) need to be entered by the user and RPHID and weight (in kg) can be entered through combo box. The present software reduces the burden of calculation and saves considerable time when number of patients to be scanned is more than 25. This software application will be instrumental in helping the user to routinely apply ALARA during dose administration in pediatric patients.

Our software application is different from that developed by Perales and Mendoza et al. Their software have two screens one to calculate pediatric dose from the weight and height of the child (or only by weight) and another screen to calculate pediatric doses from the patient’s weight and the RPH, according to EANM 2007 pediatric dosage card and that software application did not automatically stored the results. Our software applications not only calculate doses for pediatric as well adults, but also stores the records. We can use the feature of Microsoft Access to filter the data based on any field in addition to the combination of two or more field (Name, Age, sex, height, weight, scanID, NMref and Date of Scan) to view a particular record. Moreover, user can also filter the data to display pediatric and adult patients separately. Another software application to calculate pediatric RPH dose is available on World Wide Web from EANM. To use this software Internet connectivity is essential. However, this application also does not store data.

There are many formulas in the literature to calculate the BSA; however, our software calculates BSA using Du Bios formula. If a user wants to calculate the RPH dose based on BSA using any formula other than Du Bios formula, our software application cannot be used. It also cannot calculate the RPH dose using the formula other than seven formulas mentioned in Table 1. These are the few limitation of this software. To view the dose administered, the user has to leave the data entry screen. When number of patients increases beyond 4000 the response of query may take a little bit longer time than the 2-3 min computational time.

CONCLUSION

The software detailed above appears to be an easy and useful method for calculation of pediatric RPH dose in routine clinical practice. This software application will help in helping the user to routinely applied ALARA principle while pediatric dose administration. It reduces the burden of calculation and saves considerable time when number of patients to be scanned is more.

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