Development of departmental standard for traceability of measured activity for I-131 therapy capsules used in nuclear medicine

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ABSTRACT

International Basic Safety Standards (International Atomic Energy Agency, IAEA) provide guidance levels for diagnostic procedures in nuclear medicine indicating the maximum usual activity for various diagnostic tests in terms of activities of injected radioactive formulations. An accuracy of ±10% in the activities of administered radio-pharmaceuticals is being recommended, for expected outcome in diagnostic and therapeutic nuclear medicine procedures. It is recommended that the long-term stability of isotope calibrators used in nuclear medicine is to be checked periodically for their performance using a long-lived check source, such as Cs-137, of suitable activity. In view of the un-availability of such a radioactive source, we tried to develop methods to maintain traceability of these instruments, for certifying measured activities for human use. Two re-entrant chambers [(HDR 1000 and Selectron Source Dosimetry System (SSDS)] with I-125 and Ir-192 calibration factors in the Department of Radiotherapy were used to measure Iodine-131 (I-131) therapy capsules to establish traceability to Mark V isotope calibrator of the Department of Nuclear Medicine. Special nylon jigs were fabricated to keep I-131 capsule holder in position. Measured activities in all the chambers showed good agreement. The accuracy of SSDS chamber in measuring Ir-192 activities in the last 5 years was within 0.5%, validating its role as departmental standard for measuring activity. The above method is adopted because mean energies of I-131 and Ir-192 are comparable.

Key words: Activity calibration, iodine-131, re-entrant chambers, standards

Introduction

International Basic Safety Standards (International Atomic Energy Agency, IAEA)[1] provide guidance levels for diagnostic procedures in nuclear medicine, indicating the maximum usual activity for various diagnostic tests in terms of injected activities of radioactive formulations. A study[2] correlating administered radiopharmaceutical activity with imaging outcome, indicates an accuracy of ±10% in injected activity. A reasonable level of accuracy in administered activities is expected also in the therapeutic use of radioisotopes,[3] because there are other variables such as uptake in organs, biological half-life, dose response in heterogenous tumors, etc. Large-volume, calibrated, pressurized re-entrant type of ion chambers with 4π geometry are being used for this purpose along with suitable electrometers. Methods for standardization of activity of brachytherapy sources’ are outlined in literature.[4-7] Some of the important characteristics of these chambers are 1) linearity, 2) re-producibility and 3) long-term stability. For quality assurance of functioning of departmental isotope calibrators, periodic checking with long-lived 137Cs check sources is recommended.[8,9] In the Department of Nuclear Medicine we do not have such a check source, therefore, there is an urgent need to develop methods to maintain traceability to these instruments, for certifying measured activities for human use. This report highlights the method we adopted to achieve the above objective.

Materials and Methods

Isotope calibrators
The Department of Nuclear Medicine has 3 re-entrant
chambers with digital reading system-2-type Mark V (CalRad, Nuclear Associates, USA) for assay of diagnostic formulations, and 1 calibrator (Veenstra Instruments, USA) routinely used for Iodine-131 therapy capsule assay. The Mark V calibrations are traceable to cardinal imaging [(Accredited Dosimetry Calibration Laboratory, (ADCL), USA]. Different isotopes can be selected by a function key on LCD control unit; and with multiplication factor 1.00, the activities are directly displayed for respective isotopes. Iodine-131 (I-131) therapy capsules are received from GE HealthCare Buchler, Amersham, UK. The activity of capsules is checked immediately upon arrival of the consignments in the department and compared with the certified activity provided by the supplier.

Activity measurement facility to establish traceability

The Department of Radiotherapy has 2 re-entrant chambers [HDR 1000, Standard Imaging, USA, and Selectron Source Dosimetry System (SSDS) chamber, Nucletron BV, Netherlands] for measurement of activities of high-dose-rate (HDR) remote-controlled after-loading Iridium-192 sources used for treatment with microSelectron (Nucletron). Table 1 compares the specifications of all the three isotope calibrators, The collection efficiency stated by the manufacturers of these chambers is, Aion= 0.9996 and 0.9960 for HDR 1000 chamber and SSDS chamber respectively; and stated uncertainty in activity measurements for both the re-entrant chambers is within ±2%.

Calibration certificates from Accredited Dosimetry Calibration Laboratories (ADCL), provided along with these instruments [Table 1], represent multiplication factors on the displayed units, to arrive at true activity of the radioisotopes during routine measurements. The overall uncertainty in the calibration as expressed in calibration certificates is ±10%. From August 2004 till February 2010, results of calibration in measuring activities of high-intensity Ir-192 sources of 12 Iridium-192 high–dose-rate brachytherapy sources with SSDS were in agreement within 0.4% ± 0.6% of stated activity. The calibration factor for SSDS (provided by PTW, Fribourg) to measure apparent activity of Ir-192 remained constant for more than 5 years (2.3×10^6 Ci/A in September,2004 and 2.31×10^6 Ci/A in September, 2009). The calibration coefficient provided for HDR 1000 re-entrant chamber is 2.36×10^11 μGy/A for beam quality I-125 (6711). The sensitivity of this chamber provided by the manufacturer is 8.7 nA/Ci. In a recent report,[10] the long-term stability of HDR 1000 chamber over a period of more than 3 years was found to be within ± 0.5%. In the above circumstances, it was decided to refer activity measurements from Mark V chamber, traceable to SSDS and HDR 1000 re-entrant chambers.

Measurement technique for establishing calibration traceability

In the absence of locally available Cs-137 standard check source, the department used the imported I-131 capsules received for thyroid treatments, to be measured simultaneously in Mark V, HDR 1000 and SSDS re-entrant chambers. Special nylon jigs were locally fabricated to fit HDR 1000 and SSDS chambers. The jigs are able to hold the Perspex tube provided for oral administration of the I-131 capsule inside the well chamber at exact position of 100% response (5.2 cm from the bottom). This had been locally checked by separate measurements. Figure 1 shows the Mark V calibrator of the Department of Nuclear Medicine. Figures 2 and 3 show the design of the nylon jigs, along with the measurement geometry. In Figure 3, both chambers can be seen in use for measuring ‘ion currents in nA with same I-131 capsule sequentially.

Calculation of activity of capsules

With Mark V chamber, activity is directly read in MBq of GBq with keyboard setting selected for I-131 isotope. For HDR 1000 chamber and SSDS chambers, the readings in ‘nA’ are converted into ‘mCi’ by multiplying with a factor 2.36 × 10^2 mCi/nA and 2.31 × 10^2 mCi/nA x {gamma ray constants ratio of Ir-192 and I-131 (4.60/2.20)}, respectively.

Table 1: Specifications of isotope-calibrators for estimation of I-131 activity

| Parameters | Mark V               | HDR 1000           | SSDS             |
|------------|----------------------|--------------------|------------------|
| Manufacturer | Nuclear Associates | Standard Imaging     | PTW              |
| Type       | Pressurized (12-bar Argon) | Vented to atmosphere | Ventilated to atmosphere |
| Electrometer | Mark V Unit          | Premier 3000       | Unidos           |
| Bias voltage | 150 V                | 300 V              | 300 V            |
| Activity range | 0.001 MBq-200 GBq | 0.37 MBq-740 GBq  | 167 MBq-740 GBq |
| Calibrated for | All isotopes  | Iodine-125        | Iridium-192      |
| Calibration factor | 1.00                  | 2.36 × 10^11 μGy/A | 2.31×10^6 Ci/A |
| Traceable to | NIST, USA            | Cardinal Imaging   | PTW, Fribourg   |
| Linearity | ± 1.0%               | ± 0.6               | ± 0.5           |
| Accuracy  | ± 3.0%               | ± 2.0%              | ± 2.0%          |
| Uncertainty in calibration | ± 10.0%               | ± 10.0%             | ± 10.0%         |
As apparent calibration factor of Ir-192 is not provided in SI units, calculation of activity is done in ‘mCi’ and converted to MBq subsequently.

### Results

The measured levels of activity of received consignments by Mark V Isotope calibrator during the last 5 years were within a limit of 10% in 89.1% for MIBG \((n=46)\) and 63.3% for Ga-67 \((n=109)\). Table 2 shows distribution of measured activities of I-131 capsules in the past. It was found that 89.7% of the capsules had activities within 10% of certificate values (stated activity on reference date). A separate analysis of measured values for I-131 capsules referred against GE HealthCare Buchler Amersham-stated activities on dispatch date, showed an agreement within \(-3.0\% \pm 4.0\%\) \((n=175)\). Table 3 gives the activities measured by Mark-V isotope calibrator (A) compared with HDR 1000 chamber (B) and SSDS (C) measurements. The percentage deviations calculated against stated activity (on reference date) corrected for measurement date, are seen in the last three columns. Good agreement (within 2% in 4/12 measurements, within 5% in 5/12 measurements and within 10% in remaining 3/12 measurements) is seen between Mark-V and other two calibrators. Therapy level activities in GBq quantities (> 4000 MBq) have shown better agreement in measured values (6 out of 12) compared to diagnostic level < 230 MBq (4 out of 12) I-131 activities. Measured readings for estimation of activity in all three re-entrant chambers were average of more than 10 observations that had standard deviation within 0.1%.

### Discussion

The above presentation has brought to light a method for validating the calibration of activity of I-131 capsules used for therapeutic administrations, in the absence of a departmental check source for nuclear medicine isotope calibrators. Clinical requirement for estimation of activity with sealed sources such as Ir-192 for remote after-loading applications is more stringent, because the therapy-planning systems works out dose distributions based on the ‘measured activity input’ at the time of each source loadings. Therefore, the data of measured activities of I-131 correlated to these re-entrant chambers will definitely ensure traceability in the institution.
Our results of all measurements have shown assayed activities to be always higher than stated values [Tables 1-3], because usually the manufacturers provide slightly higher activities for the use of patients (to avoid cancellations due to less activities than prescribed). An earlier report, has indicated differences in activities at the department level, when compared to values quoted by manufacturers, and also various earlier reports have emphasized need for accuracy of the department calibrators.

The I-125 calibration factor is provided by Standard Imaging (ADCL) based on the TG 43 recommendations of American Association of Physicists in Medicine (AAPM). This expresses ‘strength U’, the definition includes specific gamma ray constant of the isotope. The calibration factor provided for HDR 1000 re-entrant chamber, viz., $2.36 \times 10^2 \frac{\mu Gy}{A}$, actually refers to ‘air kerma strength’ U as in TG-43 report. Taking $\Gamma = 0.0358 \frac{\mu Gy}{m^2 \cdot MBq \cdot h^4}$ (Ref. TG-43); and $37 MBq/mCi$, the conversion factor for HDR 1000 to measure I-131 activity in mCi works out to $2.59 \times 10^3 \frac{mCi}{nA}$ (gamma ray constants ratio of I-131 and I-125, 2.20/1.51). In all our measurements, we have applied numerically $2.36 \times 10^3 \frac{mCi}{nA}$ for HDR 1000 calibrator, which is 9.0% less than the calculated value of $2.59 \times 10^3 \frac{mCi}{nA}$. It is thought that this may be empirically due to difference because of low-energy gamma 31.4 KeV for I-125 compared to 364 KeV for I-131, which may be due to difference in interactions in the chamber wall materials.

The uncertainty in calibration [Table 1] describes the dispersion of the measured values of activity. Type A uncertainties are usually evaluated by statistical methods, and type B uncertainties are based on scientific judgements of non-statistical values, usually influenced by application of correction factors or physical data obtained from literature. Type B uncertainties can be derived by estimating the limit beyond which the value of the factor is not going to lie. Based on similar estimates, an earlier report, indicates an RMS error of 0.11% ($n = 100$) for SSDS isotope calibrators for measurements of HDR Ir-192 sources. The present activity estimates lie well within acceptable limits of uncertainties.

The results of this work have clearly brought out that using a selected number of I-131 sources as transfer check source, the response of two other calibrators could be ‘standardized’ as reference instruments at institutional level. This methodology could be adopted in many institutions, as most of the radiotherapy centers have high-dose-rate after-loading machines and a brachytherapy calibrator for activity calibration. Weekly measurements in these Ir-192 calibrators are being undertaken for quality assurance of high dose rate brachy machines, validating them as departmental standards.

Therefore, this report may indicate a method to routinely check nuclear medicine calibrators, as mean energy of Ir-192 is around 370 KeV, which is comparable to 364 KeV of I-131.

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