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Comparison of ^{18}F activity measurements at the VNIIM, NPL and the ENEA-INMRI using the SIRTI of the BIPM

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HIGHLIGHTS

- The SIRTI for activity comparisons of short-lived radionuclides was extended to ^{18}F.
- The three first ^{18}F SIRTI comparisons took place at the VNIIM, NPL and the ENEA-INMRI.
- Relative uncertainties of the NMIs primary measurements ranged from 0.3% to 0.6%.
- Relative uncertainties of the SIRTI measurements ranged from 0.06% to 0.14%.
- The comparison results agree with the SIR KCRV within 1 or 2 standard uncertainties.

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ABSTRACT

In 2014, the first three comparisons of activity measurements of ^{18}F were carried out at the VNIIM, NPL and the ENEA-INMRI using the BIPM's Transfer Instrument of the International Reference System. The transfer instrument and the NMIs primary measurement methods are briefly described. The degrees of equivalence with the key comparison reference value defined in the frame of the corresponding SIR comparison have been evaluated. World-wide consistency of activity measurements of ^{18}F is demonstrated.

1. Introduction

Very short-lived (much less than one day) radionuclides are essential for nuclear medicine, particularly for imaging. The use of nuclear medicine is increasing with the accessibility of these radionuclides, which is of great interest to National Metrology Institutes (NMIs) in terms of the standardization and traceability to the International System of Units (SI). However, sending ampoules of short-lived radioactive material to the BIPM for measurement in the International Reference System (SIR) (Ratel, 2007) is only practical for NMIs that are based in Europe. Consequently, to extend the usefulness of the SIR and to enable other NMIs to participate in SIR activity comparisons, a transfer instrument (SIRTI) was developed at the BIPM (Michotte et al., 2013a) with the support of the Transfer Instrument Working Group of the Consultative Committee for Ionizing Radiation Section II: Measurement of radionuclides [CCRI(II)]. The SIRTI has been in use since 2009 for comparisons of ^{99m}Tc world-wide (see for example Michotte et al., 2013b, Michotte et al., 2014a). Recently, the SIRTI has been extended to the measurement of ^{18}F, a radionuclide widely used for positron emission tomographic (PET) scans; the first comparison results are presented here. This comparison, known as BIPM.RI(II)-K4.F-18 in the key comparison database (KCDB) of the CIPM Mutual Recognition Arrangement (CIPM, 1999), is linked to the BIPM.RI(II)-K1.F-18 comparison based on the SIR through the calibration of the SIRTI against the SIR at the BIPM for ^{18}F (Michotte et al., in preparation). Therefore, degrees of equivalence of the BIPM.RI(II)-K4.F-18 comparison results with the Key Comparison Reference Value (KCRV), defined in the frame of the BIPM.RI(II)-K1.F-18 comparison, can be evaluated and included in the KCDB.

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In view of the simple decay scheme, the standardization of ^{18}F is relatively straightforward apart from the short half-life of less than two hours. The participants in the present comparison used the coincidence method (with liquid scintillation in the beta channel), the Triple-to-Double-Coincidence-Ratio (TDCR) method or 4πγ(NaI(Tl)) counting. It is worth noting that all measurement results rely on the branching ratio for the β^+ decay.

2. An overview of the SIRTI (Michotte et al., 2013a; Michotte, 2014b)

The SIRTI was developed for the comparison of activity measurements of ^{99m}Tc and has recently been extended for the measurement of ^{18}F. It is based on a 7.6 cm × 7.6 cm well-type NaI(Tl) crystal which is taken to the participant NMI for the on-site measurement of a ^{18}F solution standardized by the NMI and contained in a SIR ampoule.

The live-time technique using the MTR2 module from the Laboratoire National d'Essai – Laboratoire National Henri Becquerel, France (LNE-LNHB) (Bouchard, 2000) is used to correct for dead-time losses. The stability of the system is monitored using a ^{94}Nb reference source ($T_{1/2}$=20 300(1600) a, see NUDAT (2010))[1] from the Institute for Reference Materials and Measurements (IRMM, Geel), which also contains the ^{93m}Nb isotope. The ^{18}F count rate above a low-energy threshold, defined by the ^{93m}Nb x-ray peak at 16.6 keV, is measured relative to the ^{94}Nb count rate above the same threshold. Once the threshold is set, a brass liner is placed in the well to suppress the ^{93m}Nb contribution to the ^{94}Nb stability measurements. The ^{18}F SIR ampoule is placed in the detector well with a PVC liner in order to stop beta particles while minimizing the production of bremsstrahlung. No extrapolation to zero energy is carried out because all the measurements are made with the same threshold setting. The SIRTI sensitivity to the threshold position is expected to be larger for ^{18}F than for ^{99m}Tc, the latter being detected mainly through photoelectric interaction. However, reproducibility measurements of the threshold setting for a ^{134}Cs ampoule (to simulate ^{18}F) demonstrated agreement to better than 2×10^{-4}.

Similarly to the SIR, a SIRTI equivalent activity A_E is deduced from the ^{18}F and ^{94}Nb counting results, and the ^{18}F activity measured by the NMI. The SIRTI equivalent activity corresponds to the inverse of the detection efficiency, i.e. A_E is the activity of the source measured by the participant divided by the ^{18}F count rate in the SIRTI expressed relative to the ^{94}Nb count rate. The possible presence of impurities in the solution should be accounted for using γ-ray spectrometry measurements carried out by the NMI. The SIRTI has been calibrated against the SIR for ^{18}F resulting in a linking ratio, L, which is used to multiply the SIRTI equivalent activity, A_E, measured at a given NMI for obtaining an SIR equivalent activity, A_e, comparison result (Michotte et al., in preparation).

3. Checks of the SIRTI at the NMIs

The reproducibility and stability of the SIRTI at the NPL and the ENEA-INMRI was checked by measuring: the count rate produced by the reference ^{94}Nb source no. 3; the threshold position (defined by the ^{93m}Nb x-ray peak); the background count rate; the frequency (1 MHz) of the oscillator for the live-time correction; and the room temperature. At the NPL, the SIRTI was stable and the background level was approximately half that of the value measured at the BIPM. At the ENEA-INMRI, however, significant fluctuations of the ^{94}Nb count rate (corrected for live-time, background and decay) were observed. The observed fluctuations in the background count rate (which was about twice the value measured at the BIPM), were thought to be due to the presence of radon in the area, but do not appear to be correlated with the ^{94}Nb results. Nevertheless, the weighted mean of all the ^{94}Nb source no. 3 corrected count rates measured at the ENEA-INMRI is 7631.7(10) s^{-1} which is in agreement with the weighted mean since the set-up of the SIRTI in March 2007, R_{2007}=7632.0(3) s^{-1}. The ^{94}Nb count rate was monitored following the return of the SIRTI to the BIPM upon completion of measurements at these NMIs, giving values that are in agreement within two standard uncertainties with R_{2007}.

Table 1
Characteristics of the ^{18}F solutions measured.

NMI	Mass (g)	Impurity[a]
VNIIM	3.587 58	^{48}V: 1.73(2) × 10^{-7}
NPL	3.576 90	None detected
ENEA-INMRI	3.649 74 3.640 67[b]	^{56}Co: 6(1) × 10^{-8} ^{57}Co: 1.0(6) × 10^{-8} ^{96}Tc: 3.2(2) × 10^{-7} traces of ^{55}Co and ^{51}Cr

[a] Ratio of the impurity activity to the ^{18}F activity at the reference date.

[b] The corresponding masses of mother solution in the ampoule are 9.005 mg and 20.022 mg, respectively.

At the VNIIM, the ^{94}Nb source No. 3 was replaced by a sealed ^{137}Cs source, with the ^{94}Nb to ^{137}Cs activity ratio measured beforehand as 4.9916(9). In addition, the ^{137}Cs x-ray peak was used to set the threshold at the position of the ^{93m}Nb x-ray peak using the relationship: x-ray peak position (^{93m}Nb) is equal to x-ray peak position (^{137}Cs) multiplied by 0.5393.[2] The room conditions were very stable. However, the weighted mean of all the ^{137}Cs count rates, corrected for live-time, background and decay, measured at the VNIIM is 1527.76(24) s^{-1}, corresponding to a ^{94}Nb count rate of 7626.7(19) s^{-1} (which is lower than R_{2007}). The ^{137}Cs count rate was monitored on the return of the SIRTI to the BIPM, giving a value of 1529.1(4) s^{-1}, corresponding to a ^{94}Nb count rate of 7633.1(25) s^{-1} (in agreement within one standard uncertainty from R_{2007}). Consequently, an additional relative uncertainty of 7.5×10^{-4} was added in the comparison uncertainty budget (see Table 4).

4. Standardization of ^{18}F at the NMIs

In all three cases, the ^{18}F solution was in the form of ^{18}F-deoxyglucose (^{18}FDG) in water. In addition, the NPL reported a NaCl concentration of 9 μg g^{-1} which has been shown by Monte-Carlo simulations to have a negligible effect on the SIRTI measurements. The mass of the solution in the ampoules measured in the SIRTI and the impurities detected by the NMIs are given in Table 1. The activity concentrations measured by the NMIs are presented in Table 2, and the uncertainty budgets are shown in Tables 3a and 3b.

Fluorine-18 decays by two competitive modes directly to the ground state of ^{18}O, namely beta-plus decay and electron capture, with relative probabilities $P_{\beta+}$=96.86(19)% and P_{ec}=3.14(19)%, respectively. The x rays and Auger electrons associated with the electron-capture transitions exhibit low energies (below

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[1] the last digits of the standard uncertainty are given in parenthesis.

[2] This value differs from the ratio of the corresponding x-ray energies because of the non-zero energy at channel zero.