

^{99}Tc NMR determination of the oxygen isotope content in ^{18}O -enriched water

Valerii P. Tarasov^{1,2}  | Gayana A. Kirakosyan^{1,2}  | Konstantin E. German^{2,3}

¹ Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninskii pr. 31, Moscow 119991, Russia

² Frumkin Institute of Physical Chemistry and Electrochemistry, Russian Academy of Sciences, Leninskii pr. 31, Moscow 119991, Russia

³ Blokhin Russian Oncological Research Center, Kashirskoe sh. 24, Moscow 115478, Russia

Correspondence

Valerii P. Tarasov, Kurnakov Institute of General and Inorganic Chemistry, Russian Academy of Sciences, Leninskii pr. 31, Moscow 119991, Russia.

Email: tarasov@igic.ras.ru

^{99}Tc NMR has been suggested as an original method of evaluating the content of oxygen isotopes in oxygen-18-enriched water, a precursor for the production of radioisotope fluorine-18 used in positron emission tomography. To this end, solutions of NH_4TcO_4 or NaTcO_4 (up to 0.28 mol/L) with natural abundance of oxygen isotopes in virgin or recycled ^{18}O -enriched water have been studied by ^{99}Tc NMR. The method is based on $^{16}\text{O}/^{17}\text{O}/^{18}\text{O}$ intrinsic isotope effects in the ^{99}Tc NMR chemical shifts, and the statistical distribution of oxygen isotopes in the coordination sphere of TcO_4^- and makes it possible to quantify the composition of enriched water by measuring the relative intensities of the ^{99}Tc NMR signals of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues. Because the oxygen exchange between TcO_4^- and enriched water in neutral and alkaline solutions is characterized by slow kinetics, gaseous HCl was bubbled through a solution for a few seconds to achieve the equilibrium distribution of oxygen isotopes in the Tc coordination sphere without distortion of the oxygen composition of the water. Pertechnetate ion was selected as a probe due to its high stability in solutions and the significant ^{99}Tc NMR shift induced by a single $^{16}\text{O} \rightarrow ^{18}\text{O}$ substitution (-0.43 ± 0.01 ppm) in TcO_4^- and spin coupling constant $^1J(^{99}\text{Tc}-^{17}\text{O})$ (131.46 Hz) favourable for the observation of individual signals of $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues.

KEYWORDS

^{18}O -enriched water, ^{99}Tc , oxygen isotope composition of water, oxygen isotope exchange, NMR, pertechnetate

1 | INTRODUCTION

Oxygen-18 enriched water is a precursor for the production of radioisotope fluorine-18 (as ^{18}F fluoride), which is then converted into radiopharmaceutical 2- ^{18}F fluoro-2-deoxy-*D*-glucose (^{18}F FDG) used in positron emission tomography (PET). Due to the high consumption of H_2^{18}O in PET centers and its high cost, the purification and recovery of enriched water after the cyclotron irradiation for further reuse in the ^{18}F FDG synthesis is a high-priority task. Therefore, there is a need to quantify the isotope composition of the recycled water.

Water is one of the most difficult chemicals in which to measure ^{18}O content. The classical method^[1] consists of equilibrating a sample of H_2O with a known amount of CO_2 , followed by determination of the ^{18}O content of the CO_2 . An improved procedure, which rules out the dilution of ^{18}O with ^{16}O , is the pyrolysis of an H_2O sample with guanidine hydrochloride leading to oxygen-18-enriched CO_2 .^[2] A rapid online technique suggested by Farquhar et al.^[3] for analysis of oxygen isotopes in nitrogen-containing organic matter and water is based on pyrolysis over nickelized carbon and conversion to carbon monoxide with subsequent mass spectrometric

measurement of the $^{18}\text{O}/^{16}\text{O}$ ratio. A yet another method of determination of oxygen-18 content of water does not require gas handling and consists of the hydrolysis of PCl_5 and measurement by gas chromatography and mass spectrometry with selected ion monitoring.^[4]

In the present paper, we report an alternative method for the evaluation of the oxygen isotope composition of water, namely, ^{99}Tc NMR.^[5,6] The suggested approach is based on the effect of the oxygen isotope composition of the TcO_4^- anion on ^{99}Tc NMR parameters. At ambient temperature, the isotope shift of ^{99}Tc NMR lines for a single $^{16}\text{O} \rightarrow ^{18}\text{O}$ substitution is -0.43 ± 0.01 ppm.^[7]

2 | MATERIALS AND METHODS

2.1 | Preparation of solutions

Two types of oxygen-18-enriched water were used: virgin H_2^{18}O from two different batches (one of them was certified to contain 0.93% ^{16}O , 0.57% ^{17}O , and 98.5% ^{18}O , pH ~6.8) and recovered enriched water from FDG synthesis with an unknown oxygen isotope composition.

Weighed portions of NH_4TcO_4 or NaTcO_4 with the natural abundance of oxygen isotopes were dissolved in weighed portions of enriched water directly in NMR tubes. Four solutions were thus prepared: Solutions A and B contained each 0.23 mol/L NH_4TcO_4 in virgin enriched water (from two different batches), and solutions C and D contained 0.28 mol/L NaTcO_4 in recovered water.

To promote equilibration of neutral TcO_4^- - H_2O systems without distortion of the oxygen composition of enriched water, gaseous HCl (produced by the reaction of NaCl with concentrated H_2SO_4) was bubbled through solutions A and D in an NMR tube for 3–5 s.

2.2 | ^{99}Tc NMR

The ^{99}Tc NMR (67.55 MHz) spectra were recorded in a magnetic field of 7.05 T on a Bruker AVANCE-II 300 spectrometer (Shared Facility Center at the Institute of General and Inorganic Chemistry, RAS) at 298 K in standard 5-mm NMR tubes. A single-pulse programme with a 60-degree pulse width (the 90-degree pulse width was 11.4 μs) was used for the excitation of the spin system. A 0.1 M KTcO_4 solution in D_2O was used for shimming. The ^{99}Tc NMR spectra were recorded first within an hour after the dissolution of the salts in enriched water and then at time intervals up to 1 year (SI = 32 k, SW = 5000 Hz). The ^{99}Tc NMR chemical shifts of the isotopologues were referenced to the signal of $\text{Tc}^{16}\text{O}_4^-$ ($\delta = 0$ ppm) in the spectrum of the same solution.

The integrated intensities (I_n) of ^{99}Tc NMR signals of the isotopologues were measured with an accuracy of about $\pm 5\%$.

Spin coupling constants $^1J(^{99}\text{Tc}-^{17}\text{O})$ were presented as the average of the distances between neighbouring components of the ^{99}Tc NMR multiplet (sextet).

2.3 | Isotope distribution and content of isotopologues

Random oxygen exchange between the tetraoxo technetium anion TcO_4^- with the natural abundance of oxygen isotopes and enriched water results in a series of $\text{Tc}^{16}\text{O}_a^{17}\text{O}_b^{18}\text{O}_c^-$ isotopologues with the coordination sphere containing up to three different oxygen isotopes. The overall number of possible isotopologues Z,

$$Z = \frac{(n + s - 1)!}{n!(s - 1)!}, \quad (1)$$

is 15, where $n = 4$ is the coordination number of the metal in the tetraoxo anion, and $s = 3$ is the number of oxygen isotopes (^{16}O , ^{17}O , ^{18}O). For a random distribution (under equilibrium conditions), probability P_n of the formation of each isotopologue is defined as^[8]

$$P_n = \frac{n!(r_{16})^a(r_{17})^b(r_{18})^c}{a!b!c!}, \quad (2)$$

where r_{16} , r_{17} , and r_{18} are the mole fractions of the oxygen isotopes ($r_{16} + r_{17} + r_{18} = 1$), and indices a , b , and c denote the numbers of the corresponding oxygen isotopes in TcO_4^- ($a + b + c = 4$, where $a, b, c = 0, 1, 2, 3, 4$). The P_n probabilities of the isotopologues are proportional to the integrated intensities of the corresponding signals in ^{99}Tc NMR spectra. Therefore, the oxygen isotope content (r_{16} , r_{17} , and r_{18}) can be determined from the integrated intensities of the corresponding ^{99}Tc NMR signals.

The natural isotope composition of the salts was taken into account in calculations of the isotope ratio in pristine oxygen-18-enriched water. At the salt concentrations used (0.23 mol/L NH_4TcO_4 and 0.28 mol/L NaTcO_4), the increase in the ^{16}O content in salt solutions was ~1.6% and ~1.8%, respectively.

2.4 | Exchange time constants

The oxygen exchange between water molecules and pertechnetate anion TcO_4^- is pH-dependent. At pH 5–7, the oxygen exchange is very slow, and it takes a few months for the system to achieve equilibrium.^[6]

The oxygen isotope composition of water was determined once equilibrium was reached. A criterion of

equilibrium for the system was the constancy of the signal intensities in time.

Oxygen exchange in the $\text{Tc}^{17}\text{O}_4^- - \text{H}_2^{16}\text{O}$ system has been previously studied by ^{17}O NMR in a magnetic field of 11.7 T at 298 K as a function of acidity at acid, neutral, and alkaline pH.^[9] It has been revealed that the oxygen exchange rate constant is a quadratic function of pH:

$$k = k_{\text{H}}[\text{H}^+]^2 + k_{\text{O}}, \text{ where } k_{\text{H}} = 3.26 \times 10^4 \text{ mol}^{-1} \cdot \text{L} \cdot \text{s}^{-1} \text{ and } k_{\text{O}} = 1 \times 10^{-8} \text{ s}^{-1}.$$

The oxygen exchange in neutral and alkaline media is very slow and occurs mainly via a dissociative mechanism. It is worth noting that a similar character of oxygen isotope exchange has been recently demonstrated in aqueous solutions of potassium permanganate.^[10]

The time evolution of the distribution of oxygen isotopes in the pertechnetate–water system is described by the first-order differential equation:

$$dN/dt = -N(t)/\tau, \quad (3)$$

where $N(t)$ is the content of an isotopologue at moment t , and τ is the exchange time constant, or the mean lifetime of an isotopologue.

The solution of Equation 3 has the form

$$N(t) = N(0) \exp(-t/\tau), \quad (4)$$

where $N(0)$ is the content of an isotopologue at the initial moment of time $t = 0$. From the change in the ^{99}Tc NMR signal intensities of the isotopologues in time, the isotope exchange time constants τ_{kn} (the subscripts k and n denote the isotope composition of the initial and next isotopologues, respectively) were evaluated by the equation

$$\tau_{kn} = -t / \ln \frac{|I_n(t) - I_n(0)|}{I_k(0)}, \quad (5)$$

where $I_n(t)$ is the signal intensity at moment t , $I_n(0)$ is the signal intensity at $t = 0$, and $I_k(0)$ is the signal intensity at $t = 0$ of the preceding isotopologue from which a given isotopologue is formally formed by the replacement of ^{16}O by ^{18}O . The sum of intensities I_n is normalized to unity. Because the content of ^{17}O in the water used was low (0.57%) and at least four of the six components of the multiplets arising from $^{99}\text{Tc} - ^{17}\text{O}$ spin coupling in pertechnetate species containing one oxygen-17 do not overlap with the ^{99}Tc NMR signals of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues (see Figure 4), we can take into account only the intensities of the latter for normalization:

$$I_0 + I_1 + I_2 + I_3 + I_4 = 1. \quad (6)$$

The intensities measured at each moment of time meet the condition of $\pm 5\%$.

3 | RESULTS

Changes in relative intensities of ^{99}Tc NMR signals corresponding to $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues in time caused by redistribution of ^{16}O and ^{18}O isotopes in the technetium coordination sphere and the contents of these species in equilibrium solutions are summarized in Tables 1–3.

In the 0.23 M NH_4TcO_4 solutions in 98.5% H_2^{18}O (solutions A and B), there are ~ 211 H_2O ($188 \text{ H}_2^{18}\text{O}$) molecules per TcO_4^- ion. In 0.28 M NaTcO_4 solutions in $\sim 74\%$ H_2^{18}O (solutions C and D), there are ~ 174 H_2O ($126 \text{ H}_2^{18}\text{O}$) molecules per TcO_4^- ion. Therefore, we consider the substitution of ^{18}O for ^{16}O in the coordination sphere of pertechnetate anion as exchange between the

TABLE 1 Relative intensities (I_n) of ^{99}Tc NMR signals of $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues as a function of time (hr) elapsed after the preparation of the solution of NH_4TcO_4 in virgin H_2^{18}O (solution A)

Time t (hr)	$I_0 \text{ Tc}^{16}\text{O}_4^-$	$I_1 \text{ Tc}^{16}\text{O}_3^{18}\text{O}^-$	$I_2 \text{ Tc}^{16}\text{O}_2^{18}\text{O}_2^-$	$I_3 \text{ Tc}^{16}\text{O}^{18}\text{O}_3^-$	$I_4 \text{ Tc}^{18}\text{O}_4^-$	$I_3:I_4$
0 ^a	93.0	7.0	–	–	–	
48	88.0	11.0	0.4	0.2	–	
168	67.0	28.0	4.4	0.4	0.1	
672	20.5	39.1	28.7	9.9	1.9	
1,200	6.5	24.1	36.5	25.5	7.4	
After bubbling HCl	–	–	0.5	11.8	87.5	1:7.4
Calculated isotopologue contents, mole fractions ^b	r_{16}^4 1.2×10^{-6}	$4r_{16}^3 \times r_{18}$ 1.4×10^{-4}	$6r_{16}^2 \times r_{18}^2$ 6.1×10^{-3}	$4r_{16} \times r_{18}^3$ 0.119	r_{18}^4 0.874	1:7.3

^aMeasurements were started within an hour after the solution was prepared.

^bFormulas for calculation of each species in equilibrium mixture are given (see Equation 2). The mole fractions of oxygen isotopes, $r_{16} = 0.033$ and $r_{18} = 0.967$, correspond to the isotope content in 98.5% H_2^{18}O corrected for the mole fraction of ^{16}O introduced with NH_4TcO_4 .

TABLE 2 Relative intensities (I_n) of ^{99}Tc NMR signals of $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues as a function of time (hr) elapsed after the preparation of the solution of NH_4TcO_4 in virgin H_2^{18}O (solution B)

Time t (hr)	$I_0 \text{ Tc}^{16}\text{O}_4^-$	$I_1 \text{ Tc}^{16}\text{O}_3^{18}\text{O}^-$	$I_2 \text{ Tc}^{16}\text{O}_2^{18}\text{O}_2^-$	$I_3 \text{ Tc}^{16}\text{O}^{18}\text{O}_3^-$	$I_4 \text{ Tc}^{18}\text{O}_4^-$	$I_3:I_4$
0 ^a	87.0	11.0	0.7	0.3	–	
48	81.0	17.0	1.4	0.6	–	
168	45.0	40.0	12.0	1.7	0.2	
672	1.0	6.4	23.1	41.1	28.2	
1,200	0.7	4.5	18.9	41.0	34.8	
4,320	–	–	0.7	13.3	86.1	1:6.5
Calculated isotopologue contents, mole fractions ^b	r_{16}^4 1.9×10^{-6}	$4r_{16}^3 \times r_{18}$ 2.0×10^{-4}	$6r_{16}^2 \times r_{18}^2$ 7.6×10^{-3}	$4r_{16} \times r_{18}^3$ 0.132	r_{18}^4 0.86	1:6.5

^aMeasurements were started within an hour after the solution was prepared.^bFormulas for calculation of each species in equilibrium mixture are given (see Equation 2). The mole fractions of oxygen isotopes $r_{16} = 0.037$ and $r_{18} = 0.963$ correspond to the oxygen isotope content in equilibrium solution B, which gives the percentage 98.1% ^{18}O and 1.9% ^{16}O in virgin H_2^{18}O -enriched water used for preparing this solution.**TABLE 3** Relative intensities (I_n) of ^{99}Tc NMR signals of $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues as a function of time (hr) elapsed after the preparation of the solution of NaTcO_4 in recycled H_2^{18}O (solution D)

Time t (hr)	$I_0 \text{ Tc}^{16}\text{O}_4^-$	$I_1 \text{ Tc}^{16}\text{O}_3^{18}\text{O}^-$	$I_2 \text{ Tc}^{16}\text{O}_2^{18}\text{O}_2^-$	$I_3 \text{ Tc}^{16}\text{O}^{18}\text{O}_3^-$	$I_4 \text{ Tc}^{18}\text{O}_4^-$	$I_2:I_3:I_4$
0 ^a	97.0	3.0	–	–	–	
168	94.1	5.9	–	–	–	
672	90.8	7.8	0.8	–	–	
1,200	86.4	11.7	1.2	0.4	–	
After bubbling HCl	0.5	5.9	23.7	42.1	27.7	1.0:1.8:1.2
Calculated isotopologue contents, mole fractions ^b	r_{16}^4 5.7×10^{-3}	$4r_{16}^3 \times r_{18}$ 6.0×10^{-2}	$6r_{16}^2 \times r_{18}^2$ 0.238	$4r_{16} \times r_{18}^3$ 0.419	r_{18}^4 0.276	1.0:1.7:1.2

^aMeasurements were started within an hour after the solution was prepared.^bFormulas for calculation of each species in equilibrium mixture are given (see Equation 2). The mole fractions of oxygen isotopes $r_{16} = 0.275$ and $r_{18} = 0.725$ correspond to the oxygen isotope content in equilibrium solution D (after the treatment with HCl), which gives the percentage 74.1% ^{18}O and 25.9% ^{16}O in recycled H_2^{18}O -enriched water used for preparing this solution.

oxygen of the pertechnetate anion and the water oxygen. Possible exchange between pertechnetate ions is not taken into account.

The natural abundance of the oxygen isotopes in the salts was taken into account in calculations of the ratio between the isotopes in the systems under consideration. The introduction of ammonium or sodium pertechnetate with the natural oxygen abundance into ^{18}O -enriched water samples was responsible for a ~1.8% increase in the content of ^{16}O in the salt solutions. It should be noted that, owing to the high sensitivity of ^{99}Tc NMR, the salt concentrations can be decreased by an order of magnitude, which will significantly reduce the contribution of the natural isotope composition in TcO_4^- anions to the isotope composition of the analyzed water.

Figure 1a–1d shows how the ^{99}Tc NMR spectra of solution A change during 1,200 hr (50 days) after the salt dissolution at room temperature. The change in the

intensity of isotopologue signals in time is caused by statistical redistribution of the ^{16}O and ^{18}O isotopes in the coordination sphere of the pertechnetate anion. Table 1 presents numerical data on the change in the content of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues in time.

From these data, we determined (by Equation 5) the exchange time constant (all estimates were performed from the spectra recorded 48 hr after the preparation): For the isotope substitution $\text{Tc}^{16}\text{O}_4^- \rightarrow \text{Tc}^{16}\text{O}_3^{18}\text{O}^-$ in solution A, τ_{01} was estimated at ~15 hr. It should be noted that analogous calculations for further substitution steps ($\text{Tc}^{16}\text{O}_3^{18}\text{O}^- \rightarrow \text{Tc}^{16}\text{O}_2^{18}\text{O}_2^-$, $\text{Tc}^{16}\text{O}_3^{18}\text{O}^- \rightarrow \text{Tc}^{16}\text{O}_2^{18}\text{O}_2^-$, etc.) lead to considerable errors in the estimation of the exchange time constant because the $\text{Tc}^{(16-18)}\text{O}_4^- - \text{H}_2^{(16-18)}\text{O}$ system is characterized by numerous consecutive and parallel isotope exchange reactions.

About 1,200 hr (50 days) after the preparation of the solution, the observed distribution of the $\text{Tc}^{(16-18)}\text{O}_4^-$

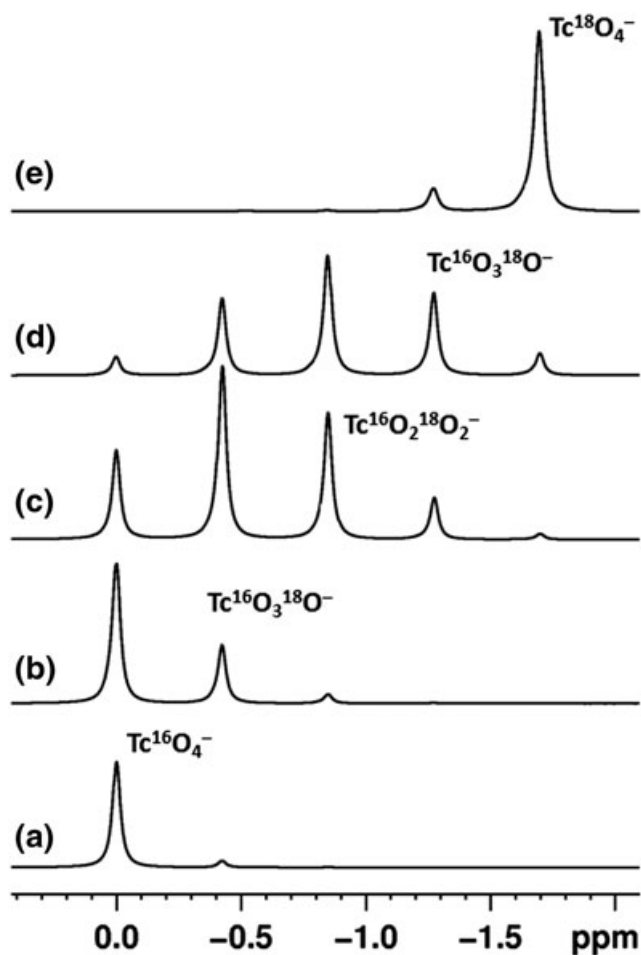


FIGURE 1 Evolution of the ^{99}Tc NMR spectrum of an NH_4TcO_4 solution in ^{18}O -enriched water (98.5% ^{18}O , solution A) in time: (a) 0, (b) 168, (c) 672, (d) 1,200 hr after preparation (before bubbling HCl), and (e) after bubbling gaseous HCl for a few seconds (equilibrium state)

species was still nonequilibrium (Figure 1d). To promote the redistribution of the oxygen isotopes, gaseous HCl was bubbled through solution A for 3–5 s (acidification with aqueous HCl was excluded in order not to distort the oxygen isotope composition), which immediately led to the equilibrium isotope distribution (Figure 1e). As is seen, the equilibrium distribution is strongly shifted towards isotopologues enriched in oxygen-18: the $\text{Tc}^{16}\text{O}^{18}\text{O}_3^-$: $\text{Tc}^{18}\text{O}_4^-$ intensity ratio is 1:7.4. From the experimentally observed mole fraction of the $\text{Tc}^{18}\text{O}_4^-$ species (0.875), the content of ^{18}O was determined to be 0.967. The contents of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues calculated by Equation 2 for $r_{16} = 0.033$ and $r_{18} = 0.967$ (Table 1) are consistent well with the experimental signal intensities in the ^{99}Tc NMR spectrum of solution A treated with HCl, which confirms a statistical distribution of the oxygen isotopes in the pertechnetate anion.^[6]

In solution B, the isotope exchange was allowed to proceed in a natural way. Figure 2a–2e shows the ^{99}Tc

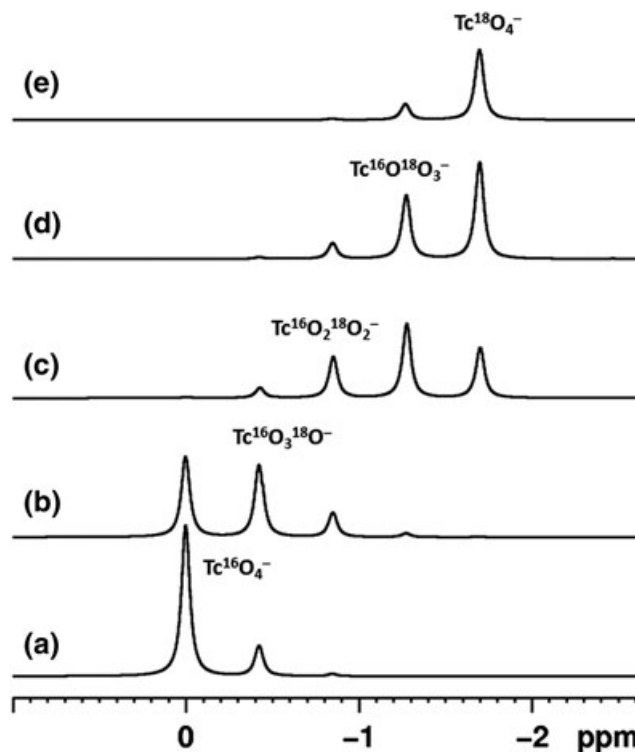


FIGURE 2 Evolution of the ^{99}Tc NMR spectrum of an NH_4TcO_4 solution in virgin ^{18}O -enriched water (solution B) in time under natural conditions: (a) 0, (b) 168, (c) 672, (d) 1,680, and (e) 4,320 hr after the preparation

NMR spectra of the solution of NH_4TcO_4 in H_2^{18}O as a function of time. It took about half a year for this solution to reach equilibrium.

Exchange time constant τ_{01} for solution B calculated by Equation 5 from the intensities measured 48 hr after the solution preparation (Table 2) was ~18 hr. As is seen from the spectra of equilibrated solutions A and B (Figure 1e and 2e), the ^{18}O -enriched water samples used for the preparation of these solutions had very close isotope compositions (Tables 1 and 2). However, the exchange rates in these two solutions are somewhat different as follows from the time evolution of the ^{99}Tc NMR spectra of solutions A and B (Figures 1 and 2). This “inconsistency” can be explained by a minor difference in pH between the water samples from different batches.

The isotope exchange in solutions C and D (0.28 M NaTcO_4 in recycled water) was characterized by an even slower kinetics than in solutions A and B in virgin enriched water (Figure 3, Table 3). The equilibrium distribution of isotopes in solution C was not reached even within a period of more than a year. In solution D, the content of isotopologues changed only slightly within ~1,200 hr after the preparation of the solution: The relative intensity of the $\text{Tc}^{16}\text{O}_4^-$ signal decreased from 0.97 to 0.864, whereas the relative intensity of the $\text{Tc}^{16}\text{O}_3^{18}\text{O}^-$ signal increased from 0.03 to 0.117. To promote the

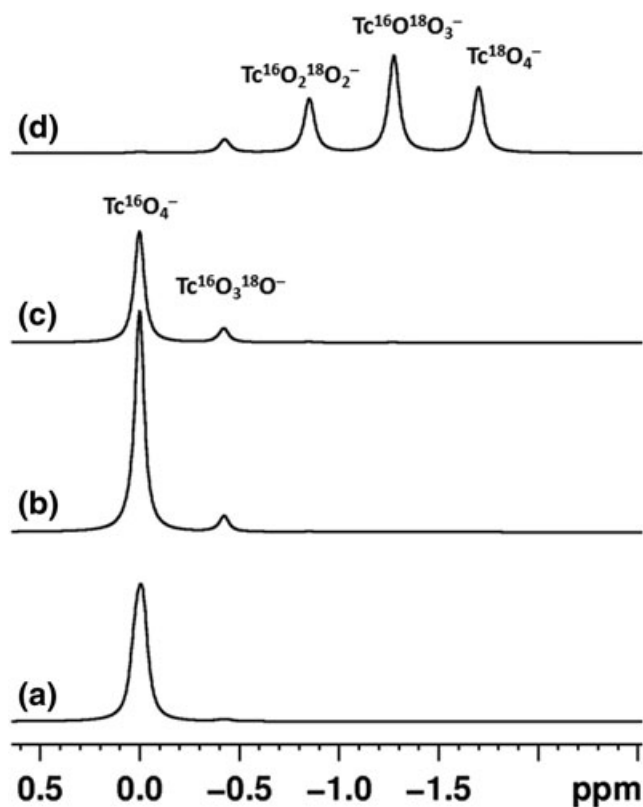


FIGURE 3 Evolution of the ^{99}Tc NMR spectrum of an NaTcO_4 solution in recycled ^{18}O -enriched water ($\sim 74\%$ ^{18}O ; solution D) in time: (a) 0, (b) 672, (c) 1,200 hr after preparation (before bubbling HCl), and (d) after bubbling gaseous HCl for a few seconds (equilibrium state)

TABLE 4 ^{99}Tc NMR isotope shifts and spin coupling constants $^1J(^{99}\text{Tc}-^{17}\text{O})$ as a function of the oxygen isotope composition of pertechnetate ion TcO_4^-

$\text{Tc}^{16}\text{O}_k^{17}\text{O}_n^{18}\text{O}_{4-k-n}$	Isotope shift, ppm (± 0.005)	$^1J(^{99}\text{Tc}-^{17}\text{O})$, Hz (± 0.20)
$\text{Tc}^{16}\text{O}_4^-$	0	—
$\text{Tc}^{16}\text{O}_3^{18}\text{O}^-$	-0.421	—
$\text{Tc}^{16}\text{O}_2^{18}\text{O}_2^-$	-0.845	—
$\text{Tc}^{16}\text{O}^{18}\text{O}_3^-$	-1.270	—
$\text{Tc}^{18}\text{O}_4^-$	-1.695	—
$\text{Tc}^{17}\text{O}^{18}\text{O}_3^-$	-1.473	130.37
$\text{Tc}^{17}\text{O}^{16}\text{O}^{18}\text{O}_2^-$	-1.063	131.64
$\text{Tc}^{17}\text{O}^{16}\text{O}_2^{18}\text{O}^-$	-0.643	132.25
$\text{Tc}^{17}\text{O}_2^{16}\text{O}^{18}\text{O}^-$	-0.872	131.40
$\text{Tc}^{17}\text{O}^{16}\text{O}_3^-$	-0.215	131.39

exchange and achieve equilibrium, solution D was treated with gaseous HCl for a few seconds. After that, the ^{99}Tc NMR spectrum ceased to change with time (Figure 3d, Table 3). Calculation by Equation 2 with taking into

account the introduction of ^{16}O with the salt demonstrated that the recovered water contained $\sim 74\%$ H_2^{18}O .

In addition to the isotopologues containing two types of oxygen isotopes, ^{16}O and ^{18}O , the spectra point to the presence of isotopologues containing ^{17}O (Table 4, Figure 4). Figure 4 shows the ^{99}Tc NMR spectrum of the equilibrium solution of NaTcO_4 in water recovered after one cycle of ^{18}F FDG synthesis containing $\sim 74\%$ H_2^{18}O (solution D). As is seen, the spectra point to the existence of isotopologues containing one ^{17}O atom (in particular, $\text{Tc}^{16}\text{O}_2^{17}\text{O}^{18}\text{O}^-$, $\text{Tc}^{16}\text{O}^{17}\text{O}^{18}\text{O}_2^-$, $\text{Tc}^{17}\text{O}^{18}\text{O}_3^-$); however, the overall content of these species was about 1% because of the low content of H_2^{17}O in the ^{18}O -enriched water. The ^{17}O nucleus has a magnetic moment ($I = 5/2$); therefore, the signal of each species containing one ^{17}O atom in the pertechnetate ion is a sextet with components of equal intensity. It is worth noting that, even if species containing more than one ^{17}O atom form in solutions, they are hardly observable at a given H_2^{17}O concentration level because of the complex multiplicity of the corresponding ^{99}Tc NMR spectra (for example, for $\text{Tc}^{16}\text{O}_2^{17}\text{O}_2^-$, the spectrum consists of 11 lines with the intensity distribution 1:2:3:4:5:6:5:4:3:2:1). Owing to the large spin coupling constant $^1J(^{99}\text{Tc}-^{17}\text{O}) = 131.46$ Hz, only two components of each sextet arising from pertechnetate ions containing one ^{17}O atom are overlapped by the signals of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ species.

It should be noted that, although pertechnetate ion is not the only possible tetraoxo anion suitable for studying the oxygen intrinsic isotope effect on the chemical shift of the central nucleus (e.g., MnO_4^- and VO_4^- are also suitable), its favourable NMR parameters (the high sensitivity, large isotope effect of the single $^{16}\text{O} \rightarrow ^{18}\text{O}$ substitution, significant spin coupling constant $^1J(^{99}\text{Tc}-^{17}\text{O})$) make this ion rather unique. A disadvantage of ^{99}Tc nucleus is that it is a weak beta-emitter (half-life 2.2×10^5 years).

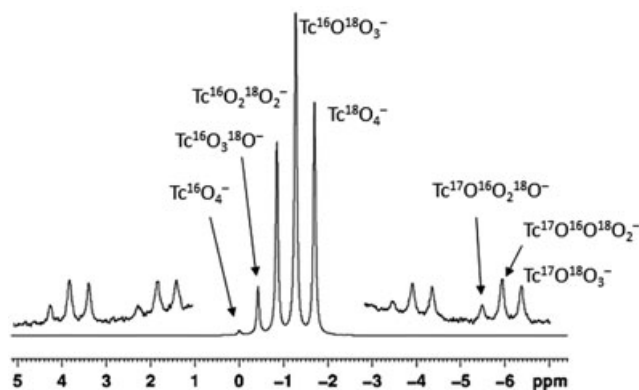


FIGURE 4 ^{99}Tc NMR spectrum at 298 K of an equilibrium 0.28 M NaTcO_4 solution in recycled water containing $\sim 74\%$ H_2^{18}O (solution D after treatment with HCl)

The isotope shift of ^{55}Mn NMR caused by a single $^{16}\text{O} \rightarrow ^{18}\text{O}$ substitution in the permanganate ion MnO_4^- is even larger than for ^{99}Tc NMR (-0.52 against -0.43 ppm), but the spin coupling constant $^1J(^{55}\text{Mn}-^{17}\text{O})$ is considerably smaller than for ^{99}Tc (~ 29 against ~ 131 Hz); therefore, at considerable content of H_2^{17}O in enriched water, its composition determined from the integrated intensities of ^{55}Mn NMR signals of the $\text{Mn}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues will be significantly distorted because of the signal overlap. An even more serious disadvantage of the permanganate ion is that it is prone to electron exchange $\text{MnO}_4^- \leftrightarrow \text{MnO}_4^{2-}$, especially in acidic solutions; this leads to line broadening and deteriorates the accuracy of measuring their integrated intensities.^[10] As distinct from MnO_4^- , pertechnetate ion TcO_4^- is very stable in aqueous media of any acidity.

4 | CONCLUSIONS

The oxygen exchange between TcO_4^- and enriched water is characterized by slow kinetics. In nearly neutral solutions ($\text{pH} \approx 6.8\text{--}7.2$), it takes on the order of hundreds of days for the $\text{Tc}^{16}\text{O}_4\text{--H}_2^{18}\text{O}$ system to reach equilibrium. Treatment of these solutions with gaseous HCl for a few seconds leads to the equilibrium distribution of oxygen isotopes in the Tc coordination sphere and does not distort the oxygen composition of the water. This fact makes it possible to quantify the composition of enriched water by measuring the relative intensities of the ^{99}Tc NMR signals of the $\text{Tc}^{16}\text{O}_{4-n}^{18}\text{O}_n^-$ isotopologues. It has been demonstrated that the suggested method based on the intrinsic oxygen isotope effect on ^{99}Tc NMR parameters and the statistical distribution of oxygen isotopes in the coordination sphere of TcO_4^- is suitable for the rapid evaluation of the composition of ^{18}O -enriched water, for example, of the recycled water after synthesis of [^{18}F]FDG for PET. The high resonance frequency of ^{99}Tc

nuclei makes it possible to use dilute solutions of pertechnetate salts ($\sim 0.01\text{--}0.02$ M).

ORCID

Valerii P. Tarasov  <http://orcid.org/0000-0003-4598-9329>

Gayana A. Kirakosyan  <http://orcid.org/0000-0002-5801-2827>

REFERENCES

- [1] M. Cohn, H. C. Urey, *J. Am. Chem. Soc.* **1938**, *60*, 679. <https://doi.org/10.1021/ja01270a052>
- [2] P. D. Boyer, D. J. Graves, C. H. Suelter, M. E. Dempsey, *Anal. Chem.* **1961**, *33*, 1906. <https://doi.org/10.1021/ac50154a036>
- [3] G. D. Farquhar, B. K. Henry, J. M. Styles, *Rapid Commun. Mass Spectrom.* **1997**, *11*, 1554. [http://onlinelibrary.wiley.com/doi/10.1002/\(SICI\)1097-0231\(199709\)11:14%3C1554::AID-RCM980%3E3.0.CO;2-I/full](http://onlinelibrary.wiley.com/doi/10.1002/(SICI)1097-0231(199709)11:14%3C1554::AID-RCM980%3E3.0.CO;2-I/full)
- [4] T. R. Sharp, R. D. Minard, *Anal. Chem.* **1980**, *52*, 598. <https://doi.org/10.1021/ac50053a060>
- [5] V. Tarasov, G. Kirakosyan, K. German, *Nucl. Med. Biol.* **2014**, *41*, 643. <https://doi.org/10.1016/j.nucmedbio.2014.05.125>
- [6] V. P. Tarasov, G. A. Kirakosyan, K. E. German, *Russ. J. Phys. Chem. B* **2015**, *9*, 185. <https://doi.org/10.1134/S1990793115020281>
- [7] V. P. Tarasov, V. I. Privalov, G. A. Kirakosyan, A. A. Gorbik, Y. A. Buslaev, *Dokl. Phys. Chem.* **1982**, *263*, 328 INIS RN 14778244.
- [8] G. Calingaert, H. A. Beatty, *J. Am. Chem. Soc.* **1939**, *61*, 2748. <https://doi.org/10.1021/ja01265a057>
- [9] S. S. Jurisson, R. K. Murmann, *Inorg. Chem.* **1999**, *38*, 3919. <https://doi.org/10.1021/ic9902830>
- [10] V. P. Tarasov, G. A. Kirakosyan, *Russ. J. Phys. Chem. B* **2016**, *10*, 582. <https://doi.org/10.1134/S1990793116040278>

How to cite this article: Tarasov VP, Kirakosyan GA, German KE. ^{99}Tc NMR determination of the oxygen isotope content in ^{18}O -enriched water. *Magn Reson Chem.* 2018;56:183–189. <https://doi.org/10.1002/mrc.4680>