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ARTICLE

Monte Carlo Simulations of Photon Specific Absorbed Fractions in a Mouse Voxel Phantom

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For preclinical assessments of several radiopharmaceuticals, photon specific absorbed fractions (SAFs) were evaluated using the voxel-based mouse phantom. The sources were assumed to be mono-energetic in the photon energy range from 10 keV to 4 MeV. The radiation transport was simulated using the Monte Carlo method. Consequently, it was confirmed that the photon SAFs for organ self-absorption are dependent on the masses of the source/target organs. It would appear that the photons SAFs for organ self-irradiation are expressed by a continuous function of photon energy emitted by the source. The photon SAFs for organ cross-irradiation might be subject to the geometry effect such as size and shape of source/target and distance between the source and target.

KEYWORDS: ***Monte Carlo, specific absorbed fractions, mouse voxel phantom***

I. Introduction

Preclinical evaluations of new radiopharmaceuticals are performed in murine, such as mouse and rat, before testing is started in humans. Understanding dose responses, radiation-related side-effects and toxicity of radiopharmaceuticals makes these studies more important since they can be translated to preclinical results for humans. Accurate dose estimates for these animals have become indispensable. In particular, mice are widely used in the preclinical examinations. Various studies have been performed on mouse organ dosimetry[1-6]. The absorbed doses of the organs were estimated by the point-kernel convolution[1,2] and the Monte Carlo method[3-6]. Organ doses can be estimated by applying the Medical Internal Radiation Dose (MIRD) method, which uses specific absorbed fractions (SAFs), the absorbed fraction in the target organ per unit mass of the target organ.

Several mathematical mouse phantoms were considered for the dosimety. A stylized mouse phantom[1-3], which used ellipsoids, spheroids and cylinders as organs, was applied to evaluate SAFs for some organs. To improve the accuracy of dosimetry, voxel mouse phantoms[4-6] which have a more realistic anatomy were developed from computed tomography (CT) and magnetic resonance imaging (MRI) data.

To perform accurate absorbed dose calculations, it may be important to use voxel phantom data with similar anatomy and size of the organs to the mouse being used in a particular experimental study. Dosimetry of mouse with different sizes seems to be worth since these animals are widely used in preclinical studies of radiopharmaceutical developments. The specific absorbed fractions of photons for self- and cross-irradiation can be used to predict mouse-organ doses. These factors are an effective tool for the preclinical dose estimates required to develop radiopharmaceuticals which emit photons. For the reasons we evaluated photon SAFs in a mouse voxel phantom using the Monte Carlo method and tabulated a new set of photon SAFs for the photon energies from 10 keV to 4 MeV.

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II. Material and methods

The general geometry setting for "Digimouse" phantom[7] was used. The Digimouse phantom was generated using co-registered micro-CT and color cryosection images of a normal nude male mouse. This phantom was developed at the University of Southern California. A matrix of 380×992×208 elements, with a voxel size of 0.1 mm was constructed. The organs segmented from these data are: whole brain, external cerebrum, cerebellum, olfactory bulbs, striatum, medulla, massetter muscles, eyes, lachrymal glands, heart, lungs, liver, stomach, spleen, pancreas, adrenal glands, kidneys, testes, bladder, skeleton and skin.

The Digimouse phantom was converted to an input file for the Monte Carlo code, EGS4[8], in conjunction with an EGS4 user code, UCSAF[9]. In the EGS4-UCSAF code, the transport of photons in the phantom was simulated and the correlations between primary and secondary particles are included. The material composition and density of the simulated organs were assumed the same as human tissues and they were taken from the report 44 of ICRU (the International Commission on Radiation Unit and Measurement)[10]. Three different tissues were considered for the mouse organs including skeleton (1.40 g/cm^3), soft tissue (1.04 g/cm^3) and lungs (0.296 g/cm^3). The mass of each organ was calculated from the number of voxels of the organ and the organ density. **Table 1** shows the mass of simulated organs of the Digimouse.

Major organs were assumed as the source and the target and the others were only considered as the targets. Each source organ was evaluated separately in order to calculate the SAFs from the absorbed energy within the organs. The source was distributed uniformly in the main organs with isotropic direction emission. Mono-energetic photon particles were simulated for the chosen source organs. Photon energies were 10, 15, 20, 30, 40, 30, 50, 100, 200, 500, 1000, 1500, 2000 and 4000 keV.

Table 1 The mass of simulated organs of the Digimouse

Organ	Organ mass (g)
Skin	1.7×10^{1}
Skeleton	1.7×10^{0}
Eye	5.8×10^{-3}
Medulla	4.8×10^{-2}
Striatum	2.7×10^{-2}
Olfactory bulbs	1.9×10^{-2}
External cerebrum	1.4×10^{-1}
Cerebellum	3.2×10^{-2}
Heart	2.3×10^{-1}
Rest of the brain	1.6×10^{-1}
Masseter muscles	1.1×10^{-1}
Lachrymal glands	3.2×10^{-2}
Bladder	2.0×10^{-1}
Testis	1.6×10^{-1}
Stomach	2.3×10^{-1}
Spleen	1.4×10^{-1}
Pancreas	4.7×10^{-2}
Liver	2.1×10^{0}
Kidneys	5.1×10^{-1}
Adrenal glands	5.9×10^{-3}
Lungs	1.2×10^{-1}

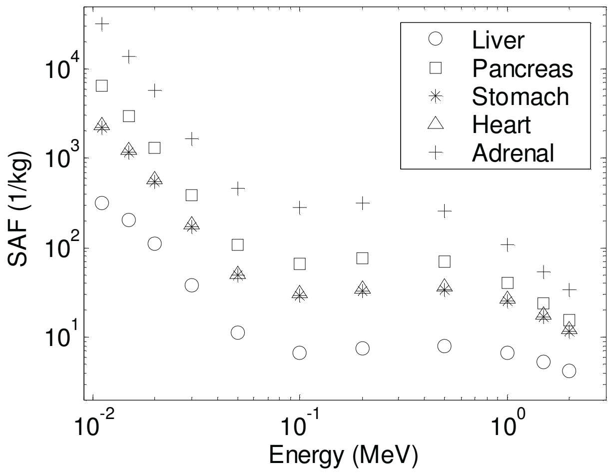

Fig. 1 Comparison of photon specific absorbed fractions for self-irradiation in some organs of the Digimouse phantom.

The photon and electron cut-offs energy were set to 1 keV and the number of histories was set sufficiently high (10^7) to reduce uncertainty less than 5%. The cross section data for photons and electrons were taken from PHOTX[11] and ICRU report 37[12], respectively.

Ⅲ.Results and discussion

Photon SAFs in eleven identified organs including skeleton, heart, bladder, testes, stomach, spleen, pancreas, liver, kidneys, adrenal glands and lungs of the Digimouse were calculated at discrete initial photons of 10 keV to 4 MeV. The photon SAFs for self- and cross-irradiation in the chosen organs are given in **Table 2**.

1. Specific absorbed fractions for self-irradiation

Figure 1 shows the photon SAFs for self-irradiation, the source organ is the target organ, for the Digimouse in the photon energy range of 10 keV to 4 MeV in liver, pancreas, stomach, heart and adrenal glands. The photon SAFs for self-irradiation decreases with increasing photon energy, except for energy range of 100 keV to 500 keV, for all organs hence it depends on photon energy. From Fig. 1 the influence of organ mass on the photon SAFs for self-irradiation can be concluded since the SAFs have different values for various organs with the same material composition and density. There are very small differences between SAFs for self-irradiation in heart and stomach, the organs with the same masses, in Fig. 1 which is attributed to the effect of organs shape on SAFs.

Figure 2 gives a favorable comparison of the photon SAFs for self-irradiation in lungs and spleen reported by Bitar *et al.*[5] with those observed in the present study. In Fig. 2, our results are entirely consistent with Bitar *et al.* [5] results. The mass of lungs and spleen in the Bitar *et al.* [5] study were 0.1228 g and 0.2164 g, respectively. The mass of lungs

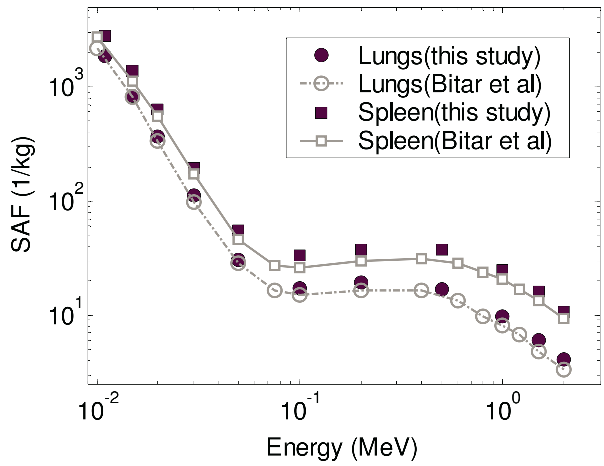

Fig. 2 Comparison of photon specific absorbed fractions for self-irradiation in the present study with Bitar *et al.* [5] study.

for our study and theirs is almost the same and the differences between the results for lungs might be originated from different density and different cross section data. The differences of two studies for spleen in all energies are higher than for lungs that confirms mass dependency of the photon SAFs for self-irradiation. Large differences between SAFs in lungs and spleen, with the mass of 0.12 and 0.14 g, confirms the effect of organ density on SAFs for self-irradiation.

2. Specific absorbed fractions for cross-irradiation

Figure 3 shows the photon SAFs for cross-irradiation, the source organ is not the target organ, in the photon energy range 10 keV to 4 MeV in stomach, pancreas, spleen, heart and adrenal glands while source is distributed in liver. The SAFs for cross-irradiation has a maximum in the photon energy range of 10 keV to 20 keV and for photons with energies higher than 100 keV the SAFs change smoothly with the photon energy. The SAFs for cross-irradiation in stomach and heart have different values in Fig. 3 regardless of the same masses. The figure shows that the SAFs for cross-irradiation do not always change with the differences in mass because of the almost same value for heart and pancreas with large mass difference (≈4.9 times). It seems that the geometry including source size, target size and their distance significantly affect on the SAFs for cross-irradiation.

Figure 4 gives comparison of the photon SAFs for cross-irradiation in spleen while bladder was source for the present study and Bitar *et al.*[5] study. From Fig. 4, we find that our results are in reasonable agreement with Bitar *et al.* results. The differences between the results of two studies might be subjected to different pathology of spleen and bladder in two different phantoms.

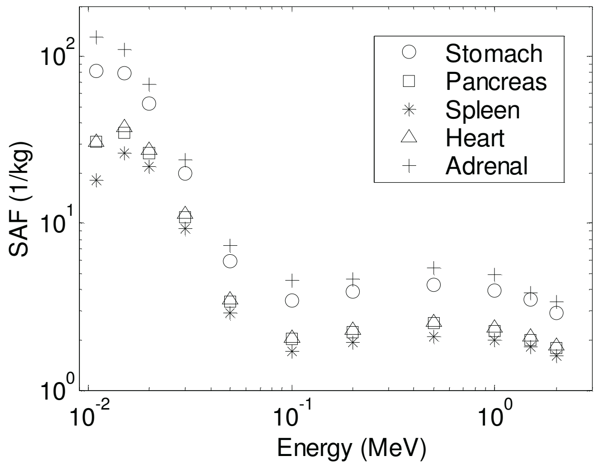

Fig. 3 Comparison of photon specific absorbed fractions for cross-irradiation in some organs of the Digimouse (source=liver).

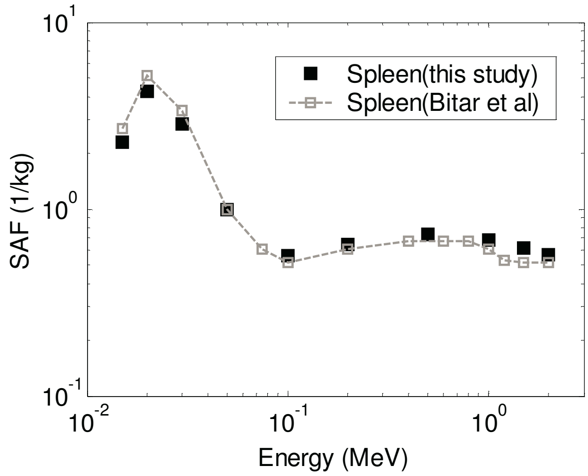

Fig. 4 Comparison of photon specific absorbed fractions for cross-irradiation in the present study with Bitar *et al.*[5] study (source =bladder).

Ⅳ. Conclusions

The specific absorbed fractions (SAFs) of photons in the Digimouse phantom were evaluated using EGS4-UCSAF code. The new set of photon SAFs were tabulated for the photon energies from 10 keV to 4 MeV in order to evaluate mouse organ doses in preclinical experiments of new radiopharmaceuticals. The photon SAFs for self-irradiation depended on the photon energy, the mass and the shape of the source organ. The photon SAFs for cross-irradiation did not always change by the mass of target and it might be affected by the source size, target size and distance between the source and target. The photon SAFs is an effective tool for the preclinical dose evaluations required to develop pharmaceuticals which emit photons.

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Table 2 Photon specific absorbed fractions (SAFs in 1/kg) in some organs of the Digimouse phantom [Energy in MeV]

Energy	Skeleton	Heart	Bladder	Testes	Stomach	Spleen	Pancreas	Liver	Kidneys	Adrenal	Lungs
	Organ source : Adrenal glands										
0.015	5.2×10^{1}	5.0×10^{0}	2.7×10^{0}	3.4×10^{-1}	6.6×10^{1}	9.9×10^{1}	1.1×10^{2}	1.1×10^{2}	1.4×10^{2}	1.4×10^{4}	1.4×10^{1}
0.1	1.5×10^{0}	7.9×10^{-1}	6.4×10^{-1}	2.8×10^{-1}	3.4×10^{0}	3.9×10^{0}	4.5×10^{0}	4.4×10^{0}	5.4×10^{0}	2.8×10^{2}	1.2×10^{0}
0.5	1.3×10^{0}	9.8×10^{-1}	8.0×10^{-1}	3.6×10^{-1}	4.1×10^{0}	4.9×10^{0}	5.5×10^{0}	5.4×10^{0}	6.7×10^{0}	2.6×10^{2}	1.5×10^{0}
1	1.2×10^{0}	9.2×10^{-1}	7.3×10^{-1}	3.4×10^{-1}	3.8×10^{0}	4.5×10^{0}	5.2×10^{0}	5.0×10^{0}	6.3×10^{0}	1.1×10^{2}	1.4×10^{0}
4	4.9×10^{-1}	6.0×10^{-1}	5.1×10^{-1}	2.3×10^{-1}	1.6×10^{0}	1.5×10^{0}	1.7×10^{0}	1.7×10^{0}	2.0×10^{0}	1.1×10^{1}	8.4×10^{-1}
	Organ source : Heart										
0.015	6.8×10^{1}	1.2×10^{3}	1.9×10^{-1}	3.7×10^{-2}	8.4×10^{0}	2.8×10^{0}	2.5×10^{0}	3.8×10^{1}	1.6×10^{0}	4.8×10^{0}	2.7×10^{2}
0.1	1.7×10^{0}	3.1×10^{1}	2.3×10^{-1}	1.2×10^{-1}	1.0×10^{0}	6.1×10^{-1}	5.7×10^{-1}	2.0×10^{0}	4.6×10^{-1}	7.8×10^{-1}	7.5×10^{0}
0.5	1.5×10^{0}	3.6×10^{1}	2.9×10^{-1}	1.5×10^{-1}	1.3×10^{0}	7.3×10^{-1}	6.9×10^{-1}	2.5×10^{0}	5.9×10^{-1}	9.7×10^{-1}	9.5×10^{0}
1	1.4×10^{0}	2.7×10^{1}	2.9×10^{-1}	1.5×10^{-1}	1.2×10^{0}	7.2×10^{-1}	6.7×10^{-1}	2.4×10^{0}	5.6×10^{-1}	8.1×10^{-1}	8.3×10^{0}
4	5.3×10^{-1}	4.4×10^{0}	1.8×10^{-1}	9.7×10^{-2}	7.7×10^{-1}	4.9×10^{-1}	4.9×10^{-1}	1.0×10^{0}	3.9×10^{-1}	6.2×10^{-1}	1.8×10^{0}
	Organ source : Kidneys										
0.015	1.8×10^{1}	1.6×10^{0}	8.1×10^{0}	1.3×10^{0}	3.7×10^{1}	7.2×10^{1}	1.9×10^{2}	3.4×10^{1}	5.9×10^{2}	1.4×10^{2}	3.6×10^{0}
0.1	9.3×10^{-1}	4.5×10^{-1}	1.1×10^{0}	4.2×10^{-1}	2.2×10^{0}	3.1×10^{0}	6.4×10^{0}	2.0×10^{0}	1.5×10^{1}	5.4×10^{0}	6.4×10^{-1}
0.5	7.8×10^{-1}	5.8×10^{-1}	1.3×10^{0}	5.5×10^{-1}	2.7×10^{0}	3.9×10^{0}	8.2×10^{0}	2.4×10^{0}	1.8×10^{1}	7.1×10^{0}	7.5×10^{-1}
1	7.4×10^{-1}	5.6×10^{-1}	1.2×10^{0}	5.1×10^{-1}	2.6×10^{0}	3.6×10^{0}	7.0×10^{0}	2.3×10^{0}	1.4×10^{1}	6.3×10^{0}	7.0×10^{-1}
4	3.9×10^{-1}	3.7×10^{-1}	7.9×10^{-1}	3.4×10^{-1}	1.2×10^{0}	1.3×10^{0}	1.9×10^{0}	1.0×10^{0}	2.7×10^{0}	1.9×10^{0}	4.7×10^{-1}
	Organ source : Liver										
0.015	3.2×10^{1}	3.8×10^{1}	2.7×10^{0}	3.6×10^{-1}	8.0×10^{1}	2.6×10^{1}	3.5×10^{1}	2.1×10^{2}	3.4×10^{1}	1.1×10^{2}	6.6×10^{1}
0.1	1.1×10^{0}	2.1×10^{0}	5.9×10^{-1}	2.4×10^{-1}	3.4×10^{0}	1.7×10^{0}	2.0×10^{0}	6.6×10^{0}	2.0×10^{0}	4.5×10^{0}	2.6×10^{0}
0.5	9.1×10^{-1}	2.5×10^{0}	7.0×10^{-1}	3.1×10^{-1}	4.2×10^{0}	2.1×10^{0}	2.5×10^{0}	7.9×10^{0}	2.4×10^{0}	5.4×10^{0}	3.2×10^{0}
1	8.4×10^{-1}	2.4×10^{0}	6.6×10^{-1}	3.3×10^{-1}	4.0×10^{0}	2.0×10^{0}	2.3×10^{0}	6.6×10^{0}	2.3×10^{0}	4.9×10^{0}	2.9×10^{0}
4	4.0×10^{-1}	1.1×10^{0}	4.6×10^{-1}	2.1×10^{-1}	1.5×10^{0}	1.0×10^{0}	1.1×10^{0}	1.9×10^{0}	1.1×10^{0}	1.7×10^{0}	1.1×10^{0}
	Organ source : Lungs										
0.015	1.1×10^{2}	2.4×10^{2}	3.0×10^{-1}	4.4×10^{-2}	1.4×10^{1}	4.7×10^{0}	3.8×10^{0}	5.9×10^{1}	3.2×10^{0}	1.2×10^{1}	8.3×10^{2}
0.1	2.1×10^{0}	7.5×10^{0}	2.3×10^{-1}	1.3×10^{-1}	1.2×10^{0}	7.0×10^{-1}	6.2×10^{-1}	2.5×10^{0}	6.0×10^{-1}	1.4×10^{0}	1.7×10^{1}
0.5	1.8×10^{0}	9.2×10^{0}	3.1×10^{-1}	1.7×10^{-1}	1.5×10^{0}	8.6×10^{-1}	7.6×10^{-1}	3.1×10^{0}	7.5×10^{-1}	1.5×10^{0}	1.7×10^{1}
1	1.5×10^{0}	8.0×10^{0}	2.9×10^{-1}	1.8×10^{-1}	1.4×10^{0}	8.1×10^{-1}	7.1×10^{-1}	2.8×10^{0}	6.8×10^{-1}	1.3×10^{0}	9.8×10^{0}
4	4.8×10^{-1}	1.7×10^{0}	2.0×10^{-1}	1.0×10^{-1}	7.6×10^{-1}	5.1×10^{-1}	5.2×10^{-1}	1.0×10^{0}	4.6×10^{-1}	8.1×10^{-1}	1.4×10^{0}
	Organ source :Pancreas										
0.015	9.8×10^{0}	2.4×10^{0}	4.6×10^{0}	1.1×10^{0}	1.7×10^{2}	3.2×10^{2}	2.9×10^{3}	3.5×10^{1}	1.9×10^{2}	1.1×10^{2}	4.3×10^{0}
0.1	7.2×10^{-1}	5.7×10^{-1}	8.0×10^{-1}	3.9×10^{-1}	6.3×10^{0}	1.0×10^{1}	6.6×10^{1}	2.0×10^{0}	6.4×10^{0}	4.5×10^{0}	6.6×10^{-1}
0.5	6.1×10^{-1}	7.1×10^{-1}	1.0×10^{0}	5.1×10^{-1}	7.8×10^{0}	1.3×10^{1}	7.0×10^{1}	2.4×10^{0}	7.9×10^{0}	5.4×10^{0}	8.0×10^{-1}
1	5.7×10^{-1}	6.6×10^{-1}	9.3×10^{-1}	4.5×10^{-1}	7.2×10^{0}	1.1×10^{1}	4.1×10^{1}	2.2×10^{0}	7.2×10^{0}	5.1×10^{0}	7.4×10^{-1}
4	3.4×10^{-1}	4.6×10^{-1}	6.5×10^{-1}	3.2×10^{-1}	2.2×10^{0}	2.7×10^{0}	5.4×10^{0}	1.1×10^{0}	1.9×10^{0}	1.6×10^{0}	5.1×10^{-1}
	Organ source :Bladder										
0.015	1.8×10^{1}	2.4×10^{-1}	1.5×10^{3}	4.6×10^{1}	2.1×10^{0}	2.3×10^{0}	4.4×10^{0}	2.7×10^{0}	8.2×10^{0}	3.3×10^{0}	3.4×10^{-1}
0.1	9.6×10^{-1}	2.2×10^{-1}	3.6×10^{1}	2.7×10^{0}	5.5×10^{-1}	5.6×10^{-1}	8.2×10^{-1}	5.8×10^{-1}	1.0×10^{0}	5.9×10^{-1}	2.4×10^{-1}
0.5	8.1×10^{-1}	2.9×10^{-1}	4.2×10^{1}	3.3×10^{0}	6.8×10^{-1}	7.3×10^{-1}	9.6×10^{-1}	7.2×10^{-1}	1.3×10^{0}	7.8×10^{-1}	3.1×10^{-1}
1	7.6×10^{-1}	2.9×10^{-1}	3.1×10^{1}	3.1×10^{0}	6.5×10^{-1}	6.8×10^{-1}	9.9×10^{-1}	6.8×10^{-1}	1.2×10^{0}	7.3×10^{-1}	2.9×10^{-1}
4	4.2×10^{-1}	1.9×10^{-1}	4.8×10^{0}	1.4×10^{0}	4.5×10^{-1}	4.7×10^{-1}	6.4×10^{-1}	4.5×10^{-1}	7.7×10^{-1}	5.1×10^{-1}	2.0×10^{-1}
	Organ source :Spleen										
0.015	1.4×10^{1}	2.8×10^{0}	2.3×10^{0}	6.4×10^{-1}	2.3×10^{2}	1.4×10^{3}	3.2×10^{2}	2.7×10^{1}	7.1×10^{1}	9.8×10^{1}	5.3×10^{0}
0.1	7.1×10^{-1}	6.1×10^{-1}	5.9×10^{-1}	3.2×10^{-1}	8.0×10^{0}	3.3×10^{1}	1.0×10^{1}	1.7×10^{0}	3.2×10^{0}	3.8×10^{0}	7.1×10^{-1}
0.5	6.3×10^{-1}	7.6×10^{-1}	7.3×10^{-1}	4.0×10^{-1}	1.0×10^{1}	3.7×10^{1}	1.2×10^{1}	2.1×10^{0}	3.9×10^{0}	4.6×10^{0}	9.0×10^{-1}
1	5.8×10^{-1}	7.0×10^{-1}	6.9×10^{-1}	3.7×10^{-1}	9.2×10^{0}	2.5×10^{1}	1.1×10^{1}	2.0×10^{0}	3.7×10^{0}	4.7×10^{0}	8.2×10^{-1}
4	3.2×10^{-1}	4.8×10^{-1}	4.7×10^{-1}	2.6×10^{-1}	2.5×10^{0}	3.9×10^{0}	2.7×10^{0}	9.9×10^{-1}	1.4×10^{0}	1.5×10^{0}	5.6×10^{-1}
	Organ source :Stomach										
0.015	1.9×10^{1}	8.4×10^{0}	2.1×10^{0}	4.0×10^{-1}	1.2×10^{3}	2.3×10^{2}	1.7×10^{2}	8.0×10^{1}	3.7×10^{1}	6.8×10^{1}	1.6×10^{1}
0.1	8.5×10^{-1}	1.0×10^{0}	5.7×10^{-1}	2.7×10^{-1}	2.9×10^{1}	8.0×10^{0}	6.4×10^{0}	3.5×10^{0}	2.2×10^{0}	3.3×10^{0}	1.2×10^{0}
0.5	7.3×10^{-1}	1.3×10^{0}	6.9×10^{-1}	3.3×10^{-1}	3.4×10^{1}	1.0×10^{1}	7.8×10^{0}	4.3×10^{0}	2.7×10^{0}	4.2×10^{0}	1.5×10^{0}
1	6.8×10^{-1}	1.2×10^{0}	6.5×10^{-1}	3.3×10^{-1}	2.5×10^{1}	9.3×10^{0}	7.3×10^{0}	4.0×10^{0}	2.5×10^{0}	4.0×10^{0}	1.4×10^{0}
4	3.7×10^{-1}	7.8×10^{-1}	4.3×10^{-1}	2.3×10^{-1}	4.2×10^{0}	2.5×10^{0}	2.2×10^{0}	1.5×10^{0}	1.2×10^{0}	1.6×10^{0}	8.2×10^{-1}