S VALUES FOR NEUROIMAGING PROCEDURES ON KOREAN PEDIATRIC AND ADULT HEAD COMPUTATIONAL PHANTOMS

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Over the past decades, the application of single-photon emission computed tomography and positron emission tomography in neuroimaging has markedly increased. In the current study, we used a series of Korean computational head phantoms with detailed cranial structures for 6-, 9-, 12-, 15-y-old children and adult and a Monte Carlo transport code, MCNPX, to calculate age-dependent specific absorbed fraction (SAF) for mono-energetic electrons ranging from 0.01 to 4 MeV and *S* values for seven radionuclides widely used in nuclear medicine neuroimaging for the combination of ten source and target regions. Compared to the adult phantom, the 6-y phantom showed up to 1.7-fold greater SAF (cerebellum < cerebellum) and up to 1.4-fold greater *S* values (vitreous body < lens) for ¹²³I. The electron SAF data, combined with our previous photon SAF data, will facilitate absorbed dose calculations for various cranial structures in patients undergoing neuroimaging procedures.

INTRODUCTION

Neuroimaging procedures provide functional information in the brain through the injection of radiopharmaceuticals, which exposes the patient to ionizing radiation but not exceeding the dose level causing deterministic effects⁽¹⁾. However, radiation dose to normal tissues should be maintained as low as possible to avoid potential stochastic late effects. To achieve the goal, it is required to determine absorbed dose⁽²⁾, i.e. the energy absorbed per unit mass (Gy) in organs or tissues of interests.

Methods to estimate the radiation dose from radiopharmaceuticals have been developed by the Medical Internal Radiation Dosimetry (MIRD) committee of the Society of Nuclear Medicine and Molecular Imaging (SNMMI)^(3, 4). According to the MIRD formalism, later harmonized with the International Commission for Radiological Protection (ICRP)⁽⁵⁾, the absorbed dose to a target region for different types of particles emitted from source regions can be estimated by the products of the time-integrated activity in each source region and organ dose coefficients for source and target pairs, called *S* values (Gy/(Bq·s)). *S* values are derived from the energy spectrum of a given radionuclide and specific absorbed fraction (SAF) calculated by Monte Carlo radiation transport methods coupled with computational human phantoms. The latest *S* values for neuroimaging procedures are based on a stylized model of the adult head and brain in the MIRD Pamphlet no. 5⁽⁶⁾, later revised in the MIRD Pamphlet no. 15⁽⁷⁾, which provided electron and photon SAFs and *S* values for 24 radionuclides.

Computational human phantoms have evolved from the simplified stylistic phantoms through voxel phantoms to surface-based phantoms that represent more realistic anatomy compared to that of the old ones⁽⁸⁾. The latest phantom format allows for more accurate estimation of radiation dose absorbed in human anatomy. Chao *et al.* reported *S* values for five brain imaging radionuclides using detailed adult head voxel phantom⁽⁹⁾. However, no *S* values from realistic head models are available for pediatric dosimetry applications to date. The optimization of the absorbed dose calculation in pediatric nuclear medicine procedures is essential considering the higher radio-sensitivity and longer life expectancy of pediatric patients compared to adult populations.

In our previous study, we developed a series of detailed age-dependent Korean computational head phantoms (6-, 9-, 12- and 15-y-old children and adult)⁽¹⁰⁾ by processing the head model of an existing Korean whole-body voxel phantom of 7-y-old as a template⁽¹¹⁾, and then provided a comprehensive set of photon SAFs. In the current study, we used the same computational head phantom series to complete our dataset of internal dose coefficients by adding electron SAFs, as well as *S* values for seven radionuclides commonly used in neuroimaging procedures.

MATERIALS AND METHODS

The age-dependent Korean head phantoms

In the current study, we employed a series of Korean computational head phantoms with detailed cranial

substructures for 6-, 9-, 12-, 15-y-old children and adult, that we previously developed⁽¹⁰⁾ by non-uniformly adjusting a template head phantom of 7-y-old child to match Korean standard age-dependent head dimensions. These age-dependent head phantoms, originally available in polygon mesh format, were converted into binary voxel format to calculate electron SAFs using Monte Carlo radiation transport. The voxel resolution of each head phantom was $1 \times 1 \times 1 \text{ mm}^3$. The detailed description of the head phantom series can be found in the previous paper⁽¹⁰⁾. The cross-sectional images of the 6-, 9-, 12-, 15-y-old children and adult head phantoms are shown in Figure 1. Masses of all organs and tissues included in the head phantoms are listed in Table 1, where the source and target organs/tissues selected for SAF and S values calculations are marked bold and italic. A comparison of the organ mass for six head structures which were found in both our adult head phantom and the MIRD Pamphlet 15⁽⁷⁾, is presented in Table 1. Percent difference between the two phantoms for these the six structures is listed in the last column.

Calculations of electron SAFs and S values

According to the MIRD formalism⁽⁵⁾, the S value ($\text{Gy}/(\text{Bq}\cdot\text{s})$) is defined as the mean absorbed dose to the target r_T per unit of cumulated activity in the source region r_S :

$$S(r_T \leftarrow r_S) = \sum_i \Delta_i \Phi(r_T \leftarrow r_S, E_i) \quad (1)$$

where Δ_i is the mean energy of the i th transition per nuclear transformation, such as $\Delta_i = Y_i E_i$, with E_i the energy emitted for radiation type i with a probability Y_i . The calculation of S values hence relies on another dosimetric quantity, the SAF, $\Phi(r_T \leftarrow r_S, E_i)$, defined as the ratio of the absorbed fraction (AF), $\phi(r_T \leftarrow r_S, E_i)$, to the mass of the target organ $M(r_T)$:

$$\Phi(r_T \leftarrow r_S, E_i) = \frac{\phi(r_T \leftarrow r_S, E_i)}{M(r_T)} \quad (2)$$

where AF $\phi(r_T \leftarrow r_S, E_i)$ represents the fraction of the energy emitted in source region r_S that is absorbed in the target region r_T .

In the current study, to calculate electron SAFs, mono-energetic electrons with the energy of 0.01, 0.015, 0.02, 0.03, 0.05, 0.1, 0.2, 0.5, 1, 1.5, 2 and 4 MeV were uniformly sampled within the 10 source organs or tissues listed in Table 1. Elemental compositions and densities of these organs or tissues were taken from the International Commission on Radiation Unit and Measurement (ICRU)⁽¹²⁾ and the ICRP Publications⁽¹³⁾.

Using the photon SAFs available from our previous publication⁽¹⁰⁾ and electron SAFs calculated from the current study, S values can be computed for any source and target pairs listed in Table 1 for each one of the 6-, 9-, 12-, 15-y-old and adult head phantoms, and for any radionuclide used in nuclear medicine, of which energy spectrum is available, for instance, in the ICRP Publication 107⁽¹⁴⁾. This indirect method to calculate S values can be implemented as an alternative to the direct calculation of S values via Monte Carlo simulation, which is widely used in patient-specific dosimetry. In the current study, S values were directly computed by using a previously-published method^(15, 16) based on Monte Carlo radiation transport techniques for seven different radionuclides commonly used in single-photon emission computed tomography (SPECT) and positron emission tomography (PET) functional neuroimaging: ^{11}C , ^{13}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$, ^{111}In and ^{123}I . All nuclear data used in this study were taken from ICRP Publication 107⁽¹⁴⁾. The main physical characteristics of these radionuclides are summarized in Table 2.

For both electron SAF and S values, two different situations can be involved: self-irradiation in an organ or a tissue, when source and target region is identical ($r_S = r_T$), and cross-irradiation from a source region to a target region, when source and target regions are different ($r_S \neq r_T$). Concerning S values for self-irradiation, non-penetrating radiation (e.g. electrons) at the scale of the organ/tissue are likely to be the major contributor to the absorbed dose.

Figure 1. 6-, 9-, 12-, 15-y-old children and adult Korean head phantoms in transversal views at the level of the lens of the eyes.

Table 1. Mass (g) of organs and tissues measured from the five age-dependent Korean head phantoms for 6-, 9-, 12-, 15-y-old children and adult (: Villoing *et al.* 2017⁽¹⁰⁾). Organs and tissues that were selected for source and target in the current study are marked bold and italic. The organ mass for the MIRD adult head phantom is also included for comparison.

Organs	Phantom age (y)					MIRD ^a
	6	9	12	15	Adult	
Skin	250.3	284.3	293.6	332.8	391.7	291.3
Fat	331.7	374.9	414.0	468.9	550.1	
Muscle	312.7	356.7	408.2	458.8	539.5	
Bone (cortical)	509.3	579.8	610.8	688.0	809.0	
<i>Eye (lens)</i>	0.3	0.4	0.4	0.4	0.5	15.8 ^b
<i>Eye (sclera)</i>	2.9	3.2	3.4	3.8	4.4	
<i>Eye (vitreous body)</i>	3.8	4.4	4.5	5.1	6.0	
Cartilage	1.3	1.5	1.8	2.0	2.3	
<i>Gray matter</i>	680.9	776.1	790.4	820.8	964.9	
<i>White matter</i>	513.5	585.1	598.0	618.7	727.0	664.8
<i>Cerebellum</i>	142.1	161.9	176.9	199.4	234.4	144.7
<i>Brainstem</i>	26.8	30.6	31.2	35.2	41.3	
<i>Spinal cord</i>	3.9	4.5	5.2	5.8	6.9	7.1
<i>Tongue</i>	9.3	10.6	12.2	13.7	16.1	
Blood	8.5	9.6	9.9	11.1	13.0	
<i>Cerebrospinal fluid</i>	43.1	48.5	46.3	52.4	62.0	74.7

^aFrom MIRD Pamphlet no. 15.

^bMass of the eyes combining the lens, sclera and vitreous body.

Table 2. Main physical characteristics of ¹¹C, ¹³N, ¹⁵O, ¹⁸F, ^{99m}Tc, ¹¹¹In and ¹²³I that were considered in the current study (source: ICRP Publication 107⁽¹⁴⁾)

Radionuclide	¹¹ C	¹³ N	¹⁵ O	¹⁸ F	^{99m} Tc	¹¹¹ In	¹²³ I
Decay half-life	20.39 m	9.965 m	122.24 s	109.77 m	6.015 h	2.8047 d	13.27 h
N emitted particles (/decay)	2.993	2.994	2.997	2.901	6.445	10.04	30.50
Mean beta particles energy (keV)	385.6–99.8%	491.8–99.8%	735.4–99.9%	249.8–96.7%	—	—	—
and abundance (/decay)							
Main photon	511.0–200.0%	511.0–200.0%	511.0–200.0%	511.0–193.5%	140.5–89.10%	245.4–94.10%	159.0–83.30%
particles energy (keV)						171.30–90.60%	27.47–46.50%
& abundance (/decay)						23.15–45.00%	27.19–25.00%
Main electron						22.96–24.00%	30.99–8.30%
particles energy (keV)						26.08–7.72%	30.94–4.28%
and abundance (/decay)						26.04–3.97%	529.0–1.39%
Main electron	—	—	—	—	119.5–8.92%	2.61–81.60%	3.09–73.40%
particles energy (keV)						19.28–10.60%	127.2–13.70%
and abundance (/decay)						1.75–86.20%	22.7–8.07%
Main electron						218.7–5.04%	154.1–1.63%
particles energy (keV)							
and abundance (/decay)							

Monte Carlo radiation transport

A general-purpose Monte Carlo radiation transport code, MCNPX version 2.7.0⁽¹⁷⁾ was used to simulate electrons within the five age-dependent head phantoms. Standard electron cross section libraries with the default energy cut-off of 0.001 MeV was used. The transport of secondary electrons and Bremsstrahlung photons were considered. To obtain adequate statistical accuracy, fifty million particle histories were simulated for the calculations of electron SAF and the *S* values for ^{99m}Tc, ¹¹¹In and ¹²³I, and ten million histories used for ¹¹C, ¹³N, ¹⁵O and ¹⁸F. The energy deposited to the 10 target organs and tissues was calculated by using *F8 Tally in MCNPX. The Biowulf High-Performance Computer installed at the National Institutes of Health (NIH) was used to conduct parallel computing of MCNPX. Monte Carlo calculations were conducted for the ten source and ten target organs, resulting in a total of 100 source and target pairs for the five age-dependent head phantoms.

RESULTS AND DISCUSSION

Electron specific absorbed fractions

SAFs (kg⁻¹) for electrons were calculated for 10 selected source and target regions listed in Table 1. Full dataset in a spreadsheet format is provided in Supplementary data. Figure 2A and B illustrates the electron SAF (cerebellum < cerebellum) and SAF (white matter < white matter), respectively, for the 6-, 9-, 12-, 15-y-old and adult head phantoms, and Figure 2C shows the SAF (white matter < cerebellum).

Electron SAFs for both self-absorption and cross-irradiation in the phantoms of younger ages were overall greater than those of older ages. Electron SAF (cerebellum < cerebellum) (Figure 2A) for the 6-y-old phantom were 1.7-fold greater at 0.01 MeV and 1.6-fold greater at 4 MeV than the adult phantom. When compared with the 12-y-old phantom, the SAFs for the 6-y-old phantom were 1.2-fold greater than those of the 12-y-old phantom at both 0.01 MeV and 4 MeV. In case of SAF (white matter < white matter) (Figure 2B), we observed trends similar to the SAF (cerebellum < cerebellum): electron SAFs (white matter < white matter) for the 6-y-old phantom were 1.4-fold at 0.01 MeV and 1.2-fold at 4 MeV greater than those of the adult phantom. In contrast to the cerebellum, electron SAFs (white matter < white matter) from the 9-, 12- and 15-y-old phantoms were very close to each other, with relative differences between 2.2% and 5.5%, for all the 12 electron energies. SAFs (white matter < cerebellum) (Figure 2C) were increasing with electron energy after about 1 MeV. Similar to the self-absorption in the cerebellum and the white matter, SAFs (white matter < cerebellum) for the 6-y-old phantom at

Figure 2. (a) SAFs (cerebellum < cerebellum), (b) SAFs (white matter < white matter) and (c) SAFs (white matter < cerebellum) as a function of electron energy for the 6-, 9-, 12-, 15-y-old and adult head phantoms.

4 MeV were also greater than those of the adult one by 2.0-fold.

Age-dependency of the electron SAFs within the eyes and substructures (the lens, the sclera, and the

vitreous body) were also evaluated. Figures 3A illustrates the electron SAFs (lens < lens) for the 6-, 9-, 12-, 15-y-old and adult head phantoms in case of self-absorption in the lens, and Figure 3B and C shows the SAFs (sclera < lens) and SAFs (vitreous body < lens), respectively.

As shown in Figure 2 for the brain structures, electron SAFs for the eyes in both self-absorption and cross-irradiation of younger ages were overall greater than those of older ages. Electron SAFs (lens < lens) (Figure 3A) for the 6-y-old phantom were 1.7-fold greater at 0.01 MeV and 1.4-fold greater at 4 MeV than those of the adult phantom. When compared with the 12-y-old phantom, SAFs (lens < lens) for the 6-y-old phantom were 1.3-fold at both 0.01 MeV and 4 MeV greater than those of the 12-y-old phantom. The SAFs (lens < lens) for the 9-, 12- and 15-y-old phantoms are nearly identical. Electron SAFs (sclera < lens) (Figure 3B) were constantly increasing with electron energy, from about 0.0 kg^{-1} below 0.02 MeV, to a maximum of 21.3 kg^{-1} at 2 MeV for the 6-y-old phantom, and maxima of 19.7, 18.7, 16.9 and 14.2 kg^{-1} at 4 MeV for the 9-, 12-, 15-y-old and adult head phantoms. At 4 MeV, the SAFs for the 6-y-old phantom were 1.5-fold greater than those of the adult phantom, and 1.1-fold greater than those of the 12-y-old phantom. Electron SAFs (vitreous body < lens) (Figure 3C) were increasing with electron energy, from $\sim 0.0 \text{ kg}^{-1}$ below 0.02 MeV, to maxima of 58.4, 52.8, 49.7, 44.0 and 35.8 kg^{-1} at 2 MeV for the 6-, 9-, 12-, 15-y-old and adult head phantoms, respectively, then decreasing after 2 MeV. At 4 MeV, the SAFs for the 6-y-old phantom were 1.4-fold greater than those of the adult phantom, and 1.1-fold greater than those of the 12-y-old phantom.

We consistently observed the greater electron SAFs in the head phantoms representing younger ages. In case of self-absorption (Figures 2A,B and 3A) for low electron energies, nearly 100% of the emitted energy is absorbed in the source organ, resulting in the AF to be unity. Then, SAFs are inversely proportional to the organ mass, which makes the SAFs for the younger age phantoms larger than those of the older age phantoms. When electron energy increases, the AFs (SAFs multiplied by target organ mass) are greater in the larger organs since more electrons released inside the source organ are absorbed in the same region due to its short range. However, the impact of the increase in organ mass for the larger head phantoms was more dominant than the increasing AFs so that resulting SAFs (Equation 2) for the larger head phantoms were smaller than those for the smaller phantoms. For example, the SAFs (cerebellum < cerebellum) at 4 MeV for the 6-y-old and adult phantoms were 5.21 and 3.32 kg^{-1} while the mass of cerebellum is 142.1 and 234.4 g (Table 1) and AFs were 0.74 and 0.78, respectively. We also observed the smaller electron SAFs in the larger head phantoms in cross-irradiation (Figures 2C

Figure 3. Specific absorbed fractions (SAFs) for the eyes and substructures as a function of electron energy for the 6-, 9-, 12-, 15-y-old and adult head phantoms: (a) SAFs (lens < lens); (b) SAFs (sclera < lens); and (c) SAFs (vitreous body < lens).

and 3B,C). The electron AFs tend to decrease when the inter-organ distance increase in the larger head phantoms whereas the target organ mass increases with the

size of the head phantoms. For example, the SAFs (white matter < cerebellum) at 4 MeV for the 6-y-old and adult phantoms were 2.84×10^{-2} and $1.47 \times 10^{-2} \text{ kg}^{-1}$ while the mass of the white matter is 513.5 and 727 g and the AFs are 0.0146 and 0.0107, respectively. In cross-irradiation SAF (vitreous body < lens) (Figure 3C), the SAFs increase for all ages with energy until they reach a maximum at about 2 MeV for all ages when the range of the electrons is approximately equal to the diameter of the vitreous body. After 2 MeV, the electron range becomes longer than the diameter of the vitreous body so that they can leave the vitreous body and reach other structures of the head.

S values for radionuclides

S values for ^{11}C , ^{13}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$, ^{111}In and ^{123}I were calculated for the five different head phantoms and for 10 selected source and target regions listed in Table 2. Full *S* value data in a spreadsheet format is provided in Supplementary data.

Figure 4 shows the *S* values (cerebellum < cerebellum) and *S* values (white matter < white matter) for ^{18}F for self-absorption. *S* values for the 6-y-old phantom were 1.6-fold and 1.4-fold greater than the adult phantom in the cerebellum and the white matter, respectively. When compared with the 12-y-old phantom, *S* values were 1.2-fold greater for the 6-y-old phantom in both the cerebellum and the white matter.

Figure 5 shows the *S* values for ^{123}I for (a) self-absorption in the lens of the eyes and (b) cross-irradiation within the eye structures. *S* values (lens < lens) of the 6-y-old phantom were 1.6-fold and 1.3-fold greater than those of the adult phantom and the 12-y-old phantom, respectively. Both *S* value (sclera < lens) and *S* value (vitreous body < lens) for the 6-y-old phantom were 1.4-fold greater than those for the adult phantom. As shown in Equation 1, *S* value is driven by the mean energy of transition per

nuclear transformation and SAF. Since *S* values are convoluted from SAFs and show the same general dependency as the mono-energetic SAFs on organ mass or inter-organ distance, we observe similar age-dependency in *S* values with that in SAFs: the small head phantoms show greater *S* values.

Comparison with other studies

We compared the electron SAFs (cerebellum < cerebellum) and SAFs (white matter < cerebellum) from our adult head phantom with those from the MIRD head and brain phantom⁷. We selected eight electron energies (0.05, 0.1, 0.2, 0.5, 1, 1.5, 2 and 4 MeV) for the comparison (Figure 6).

The ratios of SAFs (cerebellum < cerebellum) from our adult head phantom to those from the MIRD phantom was on average $0.63 \pm 0.02\sigma$, across

Figure 4. *S* values for ^{18}F in case of self-absorption in the cerebellum (left) and the white matter (right), for the 6-, 9-, 12-, 15-y-old and adult head phantoms.

Figure 5. *S* values for ^{123}I in cases of (a) self-absorption in the lens and (b) cross-irradiation from the lens to the sclera and to the vitreous body, for the 6-, 9-, 12-, 15-y-old children and adult head phantoms.

the eight electron energies: the SAFs from our head phantom were smaller than those from the MIRD phantom. This discrepancy can be explained by the difference in the mass of the cerebellum (Table 1): 234.4 g (our phantom) vs. 144.7 g (MIRD). The SAFs (white matter < cerebellum) from the two head phantoms also showed significant discrepancies: an average ratio of SAFs from our phantom to those from the MIRD of $1.56 \pm 1.11\sigma$, across the eight electron energies. The ratio changes depending on the energies, which may be affected by several differences between the two calculations including inter-organ distances in the head phantoms, Monte Carlo transport methods (MCNPX vs. EGS), contributions from Bremsstrahlung radiation generated at high energies. Although the ratio is up to about 4-fold, AFs are very small (<0.1%) in both phantoms.

We also compared the electron SAFs (lens < lens) and AFs (lens < lens) from our adult head phantom representing both male and female with those from the ICRP/ICRU reference adult male and female

voxel phantoms⁽¹⁸⁾. The ratios of SAFs (our data divided by ICRP) averaged across the electron energies for adult male and female are 0.82 ± 0.03 and 0.81 ± 0.02 , respectively. The discrepancies can be explained by the difference in the mass of the lens between the phantoms: 0.5 g (our adult phantom) vs. 0.38 g (ICRP adult male) and 0.4 g (ICRP adult female). This is confirmed by the comparison of AFs, where the impact of the mass is removed: the average ratios for the adult male and female, 1.03 ± 0.04 and 1.01 ± 0.03 , respectively.

We compared S values obtained from our adult head phantom with those from the MIRD head and brain phantom, for all radionuclides in common between the two studies: ^{11}C , ^{13}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$ and ^{123}I : when source is in the cerebellum (Figure 7A) and white matter (Figure 7B), and the cerebellum and white matter are targets.

In case of self-absorption in the cerebellum and white matter, the ratios of S values from our adult head phantom to those from the MIRD phantom,

Figure 6. Comparison of (a) electron SAFs (cerebellum < cerebellum) and (b) electron SAFs (white matter < cerebellum) between our adult head phantom and the MIRD head phantom.

Figure 7. Ratio of S values from our adult head phantom to those from the MIRD phantom for ^{11}C , ^{13}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$ and ^{123}I when source is in (a) the cerebellum and (b) the white matter.

averaged overall radionuclides, was $0.64 \pm 0.02\sigma$ and $0.83 \pm 0.01\sigma$, respectively. The ratio of *S* values (white matter < cerebellum), which is supposed to be equivalent to *S* values (cerebellum < white matter), from our adult head phantom to those from the MIRD was $0.80 \pm 0.01\sigma$, averaged over the six radionuclides. The *S* values from our head phantom were overall smaller than those from the MIRD phantom for SPECT and PET neuroimaging procedures mainly due to the differences in the target organ mass for self-absorption and inter-organ distances for cross-fire.

CONCLUSION

We employed a previously published series of Korean computational head phantoms with detailed cranial substructures representing 6-, 9-, 12-, 15-y-old children and adult, to calculate a comprehensive SAF values for internal electron sources (0.01–4 MeV). We also computed *S* values for seven radionuclides widely used for SPECT and PET functional neuroimaging procedures. We confirmed that the head phantoms for younger ages overall showed greater electron SAFs compared to the phantoms for older ages. Full dataset of electron SAF and *S* values for ^{11}C , ^{13}N , ^{15}O , ^{18}F , $^{99\text{m}}\text{Tc}$ and ^{123}I are available in a spreadsheet format. The combination of this comprehensive electron SAFs with previously-published photon SAFs will facilitate absorbed dose calculations for various cranial substructures in patients undergoing cranial neuroimaging procedures.

SUPPLEMENTARY MATERIAL

Supplementary material can be found at *Radiation Protection Dosimetry* online

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