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Original paper

Gallium-67 SPECT-CT for the evaluation of head and neck: preliminary study on maximum standardised uptake value in lesions, and in the parotid and submandibular glands

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Abstract

Purpose: The aim of this study was to investigate the gallium-67 (^{67}Ga) single-photon emission-computed tomography (SPECT-CT) for the evaluation of head and neck, especially maximum standardised uptake value (SUV_{max}) in lesions, and in the parotid and submandibular glands.

Material and methods: Fourteen patients with head and neck lesions who underwent SPECT-CT at 72 hours after injection of ^{67}Ga were included in this study. The ^{67}Ga SPECT-CT parameters SUV_{max} were compared between the parotid glands and submandibular glands. Statistical analyses for the SUV_{max} were performed by Mann-Whitney *U* test. A *p* value lower than 0.05 was considered as statistically significant.

Results: Of all 14 patients, ^{67}Ga SPECT-CT was positive for two cases (one malignant lymphoma and one osteomyelitis). The SUV_{max} for malignant lymphoma and osteomyelitis were 11.21 and 10.95, respectively. Furthermore, SUV_{max} for parotid glands and submandibular glands of all patients were 4.86 ± 1.89 and 4.64 ± 1.64, respectively ($p = 0.694$).

Conclusions: This study investigated the ^{67}Ga SPECT-CT for the evaluation of head and neck, especially SUV_{max} of lesions, and the parotid and submandibular glands. ^{67}Ga SPECT-CT may be an effective technique for the evaluation of maxillofacial lesions.

Key words: gallium radioisotopes, SPECT/CT, carcinoma, inflammation, salivary gland.

Introduction

Gallium-67 (^{67}Ga) scintigraphy is a useful adjunct tool for differentiation of malignant tumours from benign tumours or inflammatory disease in the oral and maxillofacial region [1-4]. ^{67}Ga scintigraphy is an effective technique for the evaluation of head and neck squamous cell carcinoma (SCC), especially tumour recurrence and distant metastases [5]. Furthermore, ^{67}Ga single-photon emission tomography (SPECT) substantially increases confidence in the diagnosis of head and neck tumours when computed tomography (CT) and/or magnetic resonance imaging (MRI) do not permit differentiation between benign and malignant disease [6]. With the exception of SCC, some authors have reported that ^{67}Ga scintigraphy is useful in the differentiation of malignant lymphoma [7], sarcoidosis [8-10], and other inflammatory diseases [11,12].

In recent years, SPECT-CT scanners provide fusion images of CT and SPECT and also produce attenuation correction maps that are necessary for quantitative analyses using the standardised uptake value (SUV) [13]. SUV is defined as the tissue concentration of tracer as measured by a scanner divided by the activity injected divided usually by body weight [14]. Quantitative salivary

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Authors' contribution:

A Study design · **B** Data collection · **C** Statistical analysis · **D** Data interpretation · **E** Manuscript preparation · **F** Literature search · **G** Funds collection

gland SPECT-CT holds promise as an objective imaging modality for assessment of salivary dysfunction [15,16]. Furthermore, SUV derived from bone SPECT-CT could be useful for the evaluation of osteonecrosis of the jaw [17,18]. However, to the best of our knowledge, ^{67}Ga SPECT-CT for the evaluation of head and neck have not been reported in the literature. The aim of this study was to investigate the ^{67}Ga SPECT-CT for the evaluation of head and neck, especially maximum standardised uptake value (SUV_{max}) in lesions, and in the parotid and submandibular glands.

Material and methods

Patients

The Ethics Committee of our institution approved this retrospective study. After providing written informed consent, 14 patients (six male, eight female; range age 25-83 years, mean age 65.1 years) underwent ^{67}Ga SPECT-CT at our university hospital from November 2018 to September 2019. The histopathological diagnoses were obtained by surgery or biopsy in all cases (three verrucous carcinoma [two tongue and one mandible], three epithelial dysplasia [one tongue, one buccal mucosa, and one floor of the mouth], one squamous cell carcinoma [tongue], one malignant lymphoma [neck], one osteoradionecrosis [mandible], one osteomyelitis [mandible], and four postoperative follow-up of malignant tumours [palatal adenoid cystic carcinoma, palatal squamous cell carcinoma, mandibular squamous cell carcinoma, and maxillary malignant melanoma]).

Image acquisition

SPECT/CT was obtained with an Optima NM/CT 640 (GE Healthcare Japan, Tokyo, Japan) at 72 hours after the injection. The radiopharmaceutical used in this study was ^{67}Ga-citrate (^{67}Ga-citrate NMP, Nihon Medi-Physics, Tokyo, Japan). Each patient was administered the agent at 111 MBq with a rapid intravenous injection. The SPECT scans were acquired using medium-energy general-purpose collimation with 93, 184, and 300 keV photoenergy peaks for ^{67}Ga, a 128 × 128 matrix of 4.2 mm pixel size, and a total of 60 projections (30 stops) over 360° with a dwell time of 20 s/stop. Subsequent to the SPECT acquisition, a low-dose CT scan was acquired with 120 kV and 20 mA using a 512 × 512 matrix. The CT data were generated with a 2.5 mm slice thickness.

Image analysis

To calculate the SUV, the SPECT/CT system was first calibrated to the dose calibrator for determination of the system sensitivity and the converting factor for radioactivity from measured counts. SUV in a given volume of interest (VOI) was indirectly calculated from the percentage of injected dose, which was obtained by using dosimetry software (Q. Metrix; GE Healthcare Japan). To derive the percentage of injected dose in a certain VOI by using dosimetry software, we entered the following information into the software in advance: the pre-injection radioactivity in the syringe and the measurement time, the post-injection residual radioactivity in the syringe and the measurement time, the time of injection to the patient, body weight, and the system sensitivity. On a dedicated workstation (GEniE Xeleris; GE Healthcare Japan), CT, SPECT, and SPECT/CT images were displayed with the dosimetry software. By using the transaxial and coronal CT images as the anatomic reference, a VOI was drawn over the lesions, the bilateral parotid gland, and the submandibular gland, which was automatically reflected on the SPECT/CT fusion images. Then the dosimetry software provided multiple quantitative data for a given VOI. The maximum SUV (SUV_{max}) in a given VOI was calculated as follows: SUV_{max} = (maximum radioactivity/voxel volume)/(injected radioactivity/body weight).

Statistical analysis

The ^{67}Ga SPECT-CT parameters of SUV_{max} were compared between the parotid glands and submandibular glands. Statistical analyses for the SUV_{max} were performed by Mann-Whitney *U* test. These analyses were performed with the statistical package IBM SPSS Statistics, version 26 (IBM Japan, Tokyo, Japan). A *p* value lower than 0.05 was considered as statistically significant.

Results

Of all 14 patients, ^{67}Ga SPECT-CT was positive for two (one malignant lymphoma [Figures 1 and 2] and one osteomyelitis [Figures 3 and 4]). The SUV_{max} for malignant lymphoma and osteomyelitis were 11.21 and 10.95, respectively. However, the other 12 patients were negative.

Table 1 shows 14 cases of ^{67}Ga SPECT-CT SUV_{max} of parotid and submandibular glands. SUV_{max} for parotid glands and submandibular glands of all patients were 4.86 ± 1.89 and 4.64 ± 1.64, respectively ($p = 0.694$). Furthermore, there was no significant relationship between age ($p = 0.544$), gender ($p = 0.320$), and SUV_{max} for parotid glands and submandibular glands.

Discussion

^{67}Ga scintigraphy has been widely used to detect various malignant neoplasms, such as SCC [1,6] and malignant lymphoma [7] of the head and neck. In our study, ^{67}Ga SPECT-CT for two of 14 patients with head and neck lesions were positive (one malignant lymphoma and one osteomyelitis). However, the other 12 patients were negative. These 12 histopathological diagnoses were three verrucous

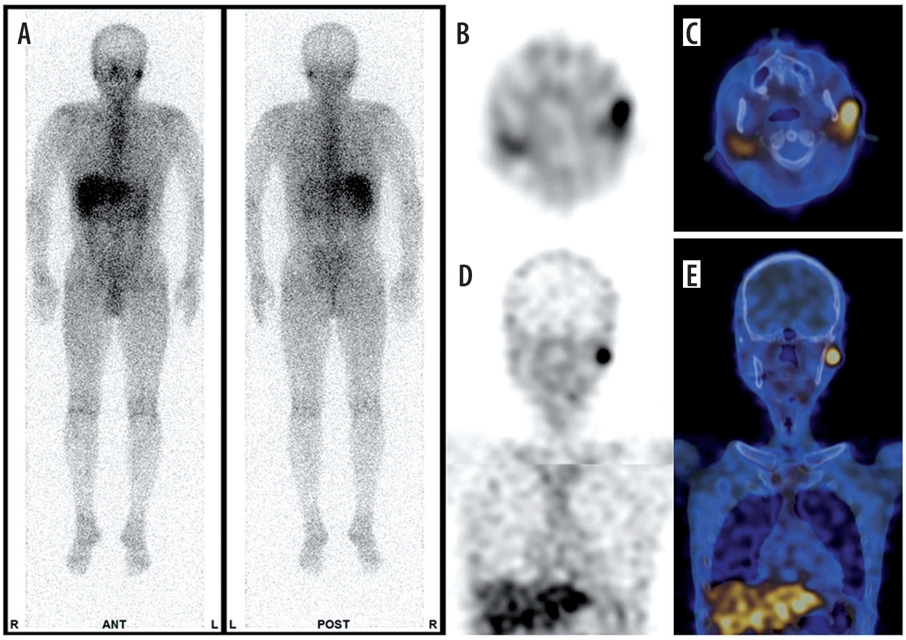

Figure 1. Malignant lymphoma of the left side of the neck in a 54-year-old male. **A)** planar, **B)** transaxial single-photon emission tomography (SPECT) and **C)** single-photon emission-computed tomography (SPECT-CT), **D)** coronal SPECT and **E)** SPECT-CT show increased uptake

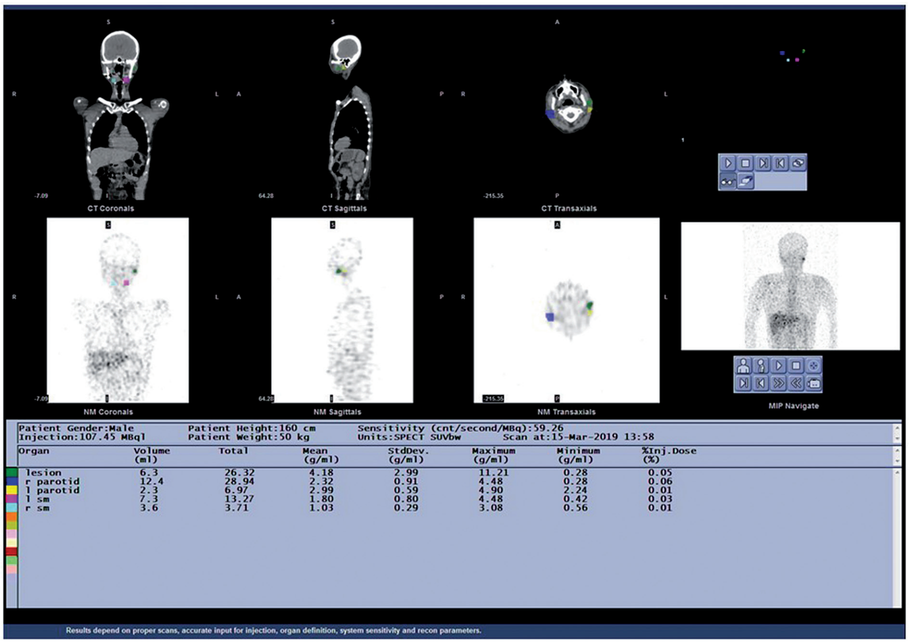

Figure 2. Malignant lymphoma of the left side of the neck in a 54-year-old male. By using the transaxial single-photon emission tomography (SPECT) and computed tomography (CT) as the anatomical reference, a volume of interest (VOI) was drawn over the lesion (green), right parotid gland (blue), left parotid gland (yellow), right submandibular gland (sky blue), and left submandibular gland (pink). The dosimetry software provided multiple quantitative data for a given VOI

carcinoma (two tongue and one mandible), three epithelial dysplasia (one tongue, one buccal mucosa, and one floor of the mouth), one squamous cell carcinoma (tongue), one osteoradionecrosis (mandible), and four postoperative follow-up of malignant tumours (palatal adenoid cystic carcinoma, palatal squamous cell carcinoma, mandibular squamous cell carcinoma, and maxillary malignant melanoma). Regarding the mechanism of ^{67}Ga accumulation in tumours, Tsan *et al.* [19] showed that ^{67}Ga was delivered to the tumour through capillaries with increased permeability, and ^{67}Ga binding proteins might also contribute to the accumulation and retention of ^{67}Ga in tumours. We consider that the size of tumours also is a factor of the degree of ^{67}Ga accumulation in lesions.

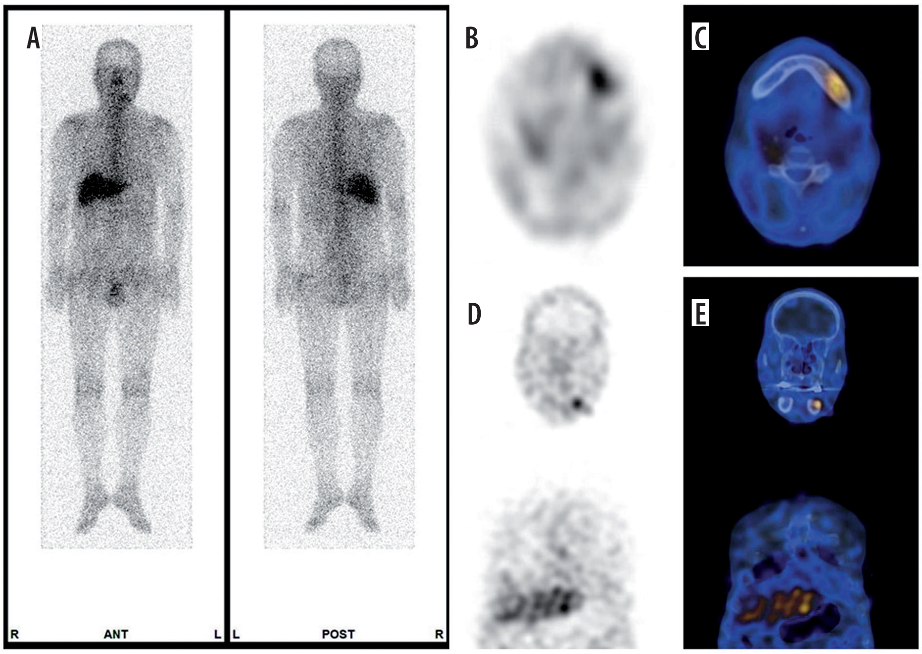

Figure 3. Osteomyelitis of the left side of the mandible in a 66-year-old male. **A)** planar, **B)** transaxial single-photon emission tomography (SPECT) and **C)** single-photon emission-computed tomography (SPECT-CT), **D)** coronal SPECT and **E)** SPECT-CT show increased uptake

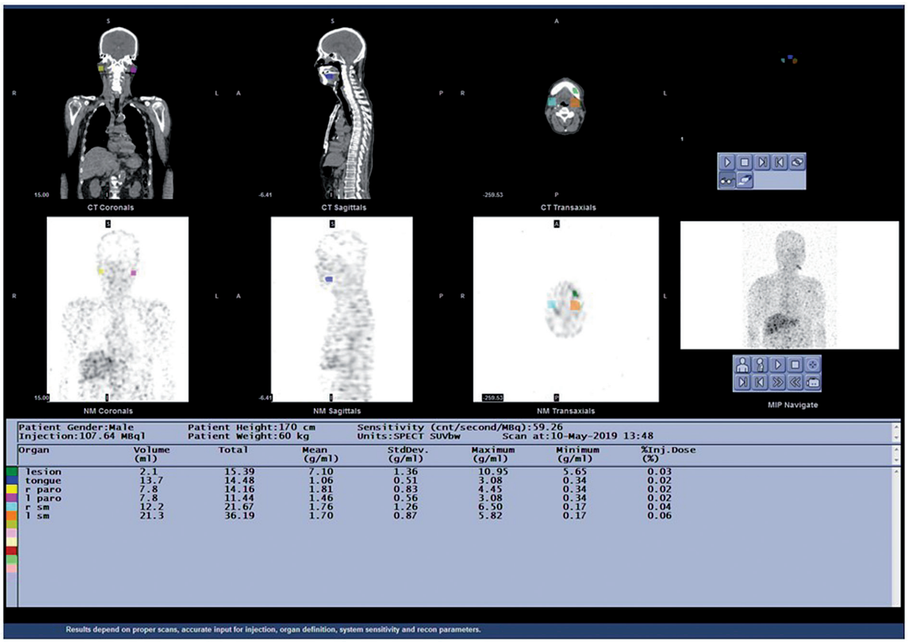

Figure 4. Osteomyelitis of the left side of the mandible in a 66-year-old male. By using the transaxial single-photon emission tomography (SPECT) and computed tomography (CT) as the anatomical reference, a volume of interest (VOI) was drawn over the lesion (green), right parotid gland (yellow), left parotid gland (pink), right submandibular gland (sky blue), and left submandibular gland (orange). The dosimetry software provided multiple quantitative data for a given VOI

Li *et al.* [1] indicated that ^{67}Ga scintigraphy for two of 11 patients who had chronic inflammatory lesions (1/4 parotitis, 1/5 submaxillaritis, and 0/2 lymphadenitis) were positive (18.2%). Tsan *et al.* [19] showed that some in tumours may be taken up by inflammatory cells when they are present. Furthermore, Keijsers *et al.* [8] showed that imaging the inflammatory activity of sarcoidosis, namely the overall sensitivity, to detect active sarcoidosis was 88% for ^{67}Ga imaging. Ishii *et al.* [9] showed that ^{67}Ga scintigraphy was useful in differentiating between sarcoidosis and IgG4-related disease. Tsai *et al.* [12] suggested that the kidney uptake index from absolute quantitative renal ^{67}Ga scintigraphy may be a useful parameter for evaluating the disease activity in lupus nephritis. Ogura *et al.*

[2-4] indicated that ^{67}Ga scintigraphy was an effective technique for detection of malignant tumours and inflammatory lesions of the head and neck. Szyszko *et al.* [20] showed the usefulness of PET-CT and PET-MRI in head and neck malignancy. However, to the best of our knowledge, ^{67}Ga SPECT-CT for the evaluation of head and neck has not been reported in the literature. Consequently, the authors consider that ^{67}Ga SPECT-CT is more useful for evaluation of malignant tumours and inflammatory diseases of the head and neck, although the successful clinical application of PET-CT and PET-MRI.

We have shown that SUV_{max} for parotid glands and submandibular glands of all patients were 4.86 ± 1.89 and 4.64 ± 1.64, respectively. We consider that the evaluation of parotid glands and submandibular glands using ^{67}Ga SPECT-CT should be useful for diagnosis and treatment planning in head and neck clinical practice.

There were several limitations to this study. The sample was relatively small. Moreover, several types of tumours and inflammatory diseases of head and neck were studied. We consider that this study is a preliminary report, and further plans regarding greater number and types of pathology in subsequent works are necessary for differential diagnosis, and reassessment of treatment and prognostic factors.

Conclusions

This study investigated the ^{67}Ga SPECT-CT for the evaluation of head and neck, especially SUV_{max} of lesions, and the parotid and submandibular glands. ^{67}Ga SPECT-CT may be an effective technique for the evaluation of maxillofacial lesions, although the successful clinical application of PET-CT and PET-MRI.

Table 1. Gallium-67 SPECT-CT maximum SUV of parotid and submandibular glands

Characteristics	Number of salivary glands	Maximum SUV		*P* value
		Mean ± SD	Range	
Salivary glands				0.694
Parotid gland	28	4.86 ± 1.89	1.73-9.24	
Submandibular gland	28	4.64 ± 1.64	1.63-8.22	
Age (years)				0.544
< 70	28	4.76 ± 1.21	3.05-7.85	
≥ 70	28	4.74 ± 2.20	1.63-9.24	
Gender				0.320
Male	24	4.87 ± 1.24	3.08-7.85	
Female	32	4.66 ± 2.08	1.63-9.24	
Total	56	4.75 ± 1.76	1.63-9.24	

SPECT – single-photon emission computed tomography, CT – computed tomography, SUV – standardised uptake value, SD – standard deviation.

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Conflict of interest

The authors declare that they have no conflict of interest.

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