Maximum and mean standardized uptake values of medication-related osteonecrosis of the jaw with bone SPECT/CT: comparison of mandibular pathologies, control and temporomandibular joints

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Research Article

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Abstract

Objectives The aim of this study was to investigate maximum and mean standardized uptake values (SUVs) of medication-related osteonecrosis of the jaw (MRONJ) with bone SPECT/CT, especially comparison of mandibular pathologies, control and temporomandibular joints.

Materials and methods Thirty-nine mandibular patients with MRONJ underwent bone SPECT/CT. The maximum and mean SUVs of the mandibular lesions using a workstation and software (Xeleris 4DR and Q. Volumetrix MI) were compared by Friedman test with Bonferroni method or Mann-Whitney U test. A p value lower than 0.05 was considered as statistically significant.

Results The maximum and mean SUVs for opposite side of the lesions (4.4 ± 2.2 and 1.7 ± 0.8) were significantly lower than those for mandibular lesions (17.5 ± 7.7, p □ 0.001 and 6.3 ± 3.0, p □ 0.001), right side of the lesions (8.1 ± 4.4, p = 0.001 and 2.9 ± 1.5, p = 0.001) and left side of the lesions (8.2 ± 4.2, p = 0.001 and 2.9 ± 1.5, p = 0.001), respectively. Furthermore, the maximum and mean SUVs of the mandibular lesions were a significant difference for age, gender, and underlying disease.

Conclusions The maximum and mean SUVs using Xeleris 4DR and Q. Volumetrix MI may be useful in clinical practice for the quantitative management of patients with MRONJ.

Clinical relevance SPECT/CT SUVs plays an important role in assessing MRONJ for the quantitative evaluation.

Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a complication of treatment with bisphosphonates and denosumab for patients with osteoporosis and bone metastases from cancer [1]. The term was defined by American Association of Oral and Maxillofacial Surgeons [2]. Single-photon emission computed tomography/computed tomography (SPECT/CT) plays an important role in assessing MRONJ [3–5]. Furthermore, SPECT/CT provide standardized uptake values (SUVs) for the quantitative evaluation of jaw lesions [6, 7].

Regarding software for the SUVs derived from bone SPECT/CT, Q. Metrix [8, 9] and GI-BONE [10–14] is useful for the quantitative analysis of jaw lesions. In recent years, a new workstation and software "Xeleris 4DR and Q. Volumetrix MI" was developed for the SUVs derived from bone SPECT/CT [15]. Q. Volumetrix MI is better than Q. Metrix at resolution, because Q. Volumetrix MI is 512 matrix; however, Q. Metrix is 256 matrix. Therefore, Q. Volumetrix MI can analyze SUVs of lesions by organ segmentation, such as the lesion, mesial, distal and opposite side as normal, using optional pan and zoom imaging. However, few reports have been published on SUVs for mandibular lesions, especially MRONJ, using Q. Volumetrix MI. The purpose of this study was to investigate maximum and mean SUVs of MRONJ using Q. Volumetrix MI, especially comparison of mandibular pathologies, control and temporomandibular joints.

Materials And Methods

Patients

The study was approved by the institutional review board of our university (approved no. ECNG-R-318), and informed consent was obtained from all individual participants included in the study. Thirty-nine mandibular patients (11 males and 28 females; mean age, 77.7 years [range, 55-91 years]) with MRONJ underwent bone SPECT/CT prior surgical treatments at our university hospital from January 2020 to December 2021. Patients were considered to have MRONJ by American Association of Oral and Maxillofacial Surgeons [2]. All patients with MRONJ were diagnosed and treated for osteoporosis or bone metastases from cancer at other hospital. Characteristics of the mandibular patients with MRONJ was shown in Table 1.

SPECT/CT imaging

SPECT/CT was performed by Optima NM/CT 640 (GE Healthcare, Tokyo, Japan) at 4 hours after injection of 740 MBq of technetium-99m hydroxymethylene diphosphonate (Tc-99m HMDP; Clear Bone Injectable, Nihon Medi-Physics, Tokyo, Japan), following our hospital protocol [6]. The SPECT was acquired using low-energy high-resolution collimation, the 140 keV photo-energy peak for Tc-99m, a 128×128 matrix of 4.2 mm pixel size, and total of 60 projections (30 stops) over 360° with a dwell time of 10 s/stop. Subsequent to the SPECT acquisition, low-dose CT was acquired with 120 kV and 20 mA using a 512×512 matrix. The CT data were generated with a 2.5 mm section thickness.

Data Analysis

The maximum and mean SUVs were obtained using a workstation and software (Xeleris 4DR and Q. Volumetrix MI, GE Healthcare, Tokyo, Japan), following our hospital protocol [15]. SPECT and CT images were displayed on the Xeleris 4DR workstation, volume of interest (VOI) using those imaging was drawn over the mandibular lesions, right, left and opposite sides of the lesions, and right and left temporomandibular joints, and the SUVs in given VOIs was analyzed (Fig. 1). The maximum and mean SUVs in given VOIs were calculated automatically as follows: maximum SUV = (maximum radioactivity / voxel volume) / (injected radioactivity / body weight) and mean SUV = (total radioactivity / VOI volume) / (injected radioactivity / body weight) (Fig. 2).

Statistical analysis

Statistical analyses for the maximum and mean SUVs, such as mandibular lesions, right, left and opposite sides of the lesion, and right and left temporomandibular joints, were compared by Friedman test with Bonferroni method. Statistical analyses for patient characteristics and the SUVs were compared by Mann-Whitney U test. A p value lower than 0.05 indicated significant differences by statistical software (IBM SPSS Statistics, version 26, IBM Japan, Tokyo, Japan).

Results

The maximum and mean SUVs of MRONJ with bone SPECT/CT was summarized in Table 2. The maximum SUV for opposite side of the lesions (4.4 ± 2.2) was significantly lower than those for mandibular lesions (17.5 ± 7.7, p 0.001), right side of the lesions (8.1 ± 4.4, p = 0.001) and left side of the lesions (8.2 ± 4.2, p = 0.001), and higher than those for right temporomandibular joints (2.5 ± 0.9, p = 0.015) and left temporomandibular joints (2.5 ± 0.8, p = 0.009). Furthermore, the mean SUV for opposite side of the lesions (1.7 ± 0.8) was significantly lower than those for mandibular lesions (6.3 ± 3.0, p 0.001), right side of the lesions (2.9 ± 1.5, p = 0.001) and left side of the lesions (2.9 ± 1.5, p = 0.001).

The patient characteristics and SPECT/CT SUVs of the mandibular lesions with MRONJ was summarized in Table 3. The maximum SUV of the mandibular lesions was a significant difference for age (p = 0.012), gender (p = 0.002), underlying disease (p = 0.021), and staging of MRONJ (p = 0.025). Furthermore, the mean SUV of the mandibular lesions was a significant difference for age (p = 0.021), gender (p = 0.001), and underlying disease (p = 0.032).

The patient characteristics and SPECT/CT SUVs of the opposite side of the lesions with MRONJ was summarized in Table 4. The maximum and mean SUVs of the opposite side of the lesions was not significant difference for age, gender, underlying disease, medication, and staging of MRONJ. Furthermore, the patient characteristics and SPECT/CT SUVs of the temporomandibular joints with MRONJ was summarized in Table 5. The maximum and mean SUVs of the temporomandibular joints was not significant difference for age, gender, underlying disease, medication, and staging of MRONJ.

Discussion

In recent years, a new workstation and software "Xeleris 4DR and Q. Volumetrix MI" was developed for the SUVs derived from bone SPECT/CT [15]. Therefore, we investigated maximum and mean SUVs of MRONJ using Q. Volumetrix MI, especially comparison of mandibular pathologies, control and temporomandibular joints.

In this study, the maximum SUV for opposite side of the lesions (4.4 ± 2.2) was significantly lower than those for mandibular lesions (17.5 ± 7.7, p 0.001), right side of the lesions (8.1 ± 4.4, p = 0.001) and left side of the lesions (8.2 ± 4.2, p = 0.001). Furthermore, the mean SUV for opposite side of the lesions (1.7 ± 0.8) was significantly lower than those for mandibular lesions (6.3 ± 3.0, p 0.001), right side of the lesions (2.9 ± 1.5, p = 0.001) and left side of the lesions (2.9 ± 1.5, p = 0.001). Miyashita et al [3, 4] indicated that 3D SPECT/CT is useful not only for detecting MRONJ but also for surgical planning. Modabber et al [16] concluded that SPECT/CT can safely detect different kinds of inflammatory jaw pathologies compared to other conventional imaging modalities; additionally, SPECT/CT assists the surgeon in determining the expansion of the process preoperatively and thereby optimizing surgery planning. We consider that the SPECT/CT SUVs using Q. Volumetrix MI showed potential as a useful parameter for evaluation of mandibular lesions, such as detecting and surgical planning.

Suh et al [17] evaluated the diagnostic accuracy of the quantitative parameter SUV at SPECT/CT for the evaluation of temporomandibular joint (TMJ) disorder (TMD), indicated that maximum SUV gradually increased from normal (2.82 ± 0.73) to mild or moderately abnormal (3.56 ± 0.76, p □ 0.05) and then to severely abnormal (4.86 ± 1.25, p □ 0.05), however, mean SUV did not vary significantly, such as 1.31 ± 0.38 for normal, 1.48 ± 0.36 for mild or moderately abnormal and 1.64 ± 0.46 for severely abnormal. In this study, the maximum SUVs of right and left TMJs were 2.5 ± 0.9 and 2.5 ± 0.8, respectively. Furthermore, the mean SUVs of right and left TMJs were 1.3 ± 0.5 and 1.3 ± 0.4, respectively. Our results seem the same as in the previous reports.

In this study, the maximum SUV of the mandibular lesions with MRONJ was a significant difference for age ($p = 0.012$), gender ($p = 0.002$), underlying disease ($p = 0.021$), and staging of MRONJ ($p = 0.025$). Furthermore, the mean SUV of the mandibular lesions was a significant difference for age ($p = 0.021$), gender ($p = 0.001$), and underlying disease ($p = 0.032$). However, the maximum and mean SUVs of the opposite side of the lesions and TMJs were not significant difference for age, gender, underlying disease, medication, and staging of MRONJ. We showed the relationship between patient characteristics with MRONJ and SUVs.

There were several limitations of this study. The sample was relatively small. Power calculation because of small sample sizes would strengthen the study, otherwise this is a significant limitation. Therefore, further research is necessary to validate these results.

Conclusions

We investigated maximum and mean SUVs of MRONJ with bone SPECT/CT, especially comparison of mandibular pathologies, control and temporomandibular joints. The maximum and mean SUVs using Xeleris 4DR and Q. Volumetrix MI may be useful in clinical practice for the quantitative management of patients with MRONJ.

Declarations

Compliance with Ethical Standards

Conflict of Interests The authors have no conflict of interest.

Funding No funding was obtained for this study.

Ethical Approval This study was approved by the Ethics Committee of The Nippon Dental University School of Life Dentistry at Niigata (ECNG-R-318).

Informed Consent The patients were informed of the scientific use of their clinical data.

Author contribution Yoshiyuki Minami and Ichiro Ogura contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Yoshiyuki Minami and Ichiro Ogura.

The first draft of the manuscript was written by Yoshiyuki Minami, and Yoshiyuki Minami and Ichiro Ogura commented on the previous versions of the manuscript. Yoshiyuki Minami and Ichiro Ogura read and approved the final manuscript.

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Tables

Table 1 Characteristics of the mandibular patients with medication-related osteonecrosis of the jaw

Patient characteristics	Number pf patients (n = 39)
Age	
80 years (55 - 79 years)	19
≧80 years (80 - 91 years)	20
Gender	
Males	11
Females	28
Underlying disease	
Osteoporosis	26
Bone metastases	13
prostate cancer	5
breast cancer	3
rectal cancer	2
kidney cancer	1
lung cancer	1
thyroid cancer	1
Medication	
Bisphosphonates	25
minodronate	10
alendronate	5
zoledronate	4
ibandronate	3
risedronate	3
Non-bisphosphonates	14
denosumab	13
bevacizumab	1
Staging of MRONJ	
Stage 1	2
Stage 2	29

Stage 3	8

MRONJ medication-related osteonecrosis of the jaw

Table 2 Maximum and mean SUVs of medication-related osteonecrosis of the jaw with bone SPECT/CT

Parameters	Mean ± SD	Range	P-value
Maximum SUV			
Mandibular lesions	17.5 ± 7.7	5.7 - 35.4	< 0.001
Right side of the lesions	8.1 ± 4.4	2.5 - 20.8	0.001
Left side of the lesions	8.2 ± 4.2	2.2 - 18.3	0.001
Opposite side of the lesions	4.4 ± 2.2	1.1 - 9.5	—
Right temporomandibular joints	2.5 ± 0.9	1.4 - 5.9	0.015
Left temporomandibular joints	2.5 ± 0.8	1.2 - 5.2	0.009
Mean SUV			
Mandibular lesions	6.3 ± 3.0	2.2 - 13.9	< 0.001
Right side of lesions	2.9 ± 1.5	1.0 - 6.8	0.001
Left side of lesions	2.9 ± 1.5	0.7 - 7.5	0.001
Opposite side of the lesions	1.7 ± 0.8	0.4 - 3.3	—
Right temporomandibular joints	1.3 ± 0.5	0.6 - 2.8	0.193
Left temporomandibular joints	1.3 ± 0.4	0.7 - 3.0	0.250

SUV standardized uptake value, *SD* standard deviation

Table 3 Patient characteristics and SPECT/CT SUVs of the mandibular lesions with medication-related osteonecrosis of the jaw

Patient characteristics	Mandibular lesions (Mean ± SD)	
	Maximum SUV	Mean SUV
Age	p = 0.012	p = 0.021
80 years (n = 19)	14.5 ± 7.1	5.5 ± 3.1
≧80 years (n = 20)	20.3 ± 7.3	7.0 ± 2.8
Gender	p = 0.002	p = 0.001
males (n = 11)	12.8 ± 8.0	4.4 ± 2.6
females (n = 28)	19.3 ± 6.8	7.0 ± 2.8
Underlying disease	p = 0.021	p = 0.032
osteoporosis (n = 26)	19.1 ± 6.9	6.7 ± 2.7
bone metastases (n = 13)	14.3 ± 8.4	5.4 ± 3.5
Medication	p = 0.133	p = 0.426
bisphosphonates (n = 25)	18.8 ± 7.4	6.4 ± 2.6
non-bisphosphonates (n = 14)	15.2 ± 8.0	6.1 ± 3.7
Staging of MRONJ	p = 0.025	p = 0.196
stage 1, 2 (n = 31)	15.8 ± 6.3	5.9 ± 2.6
stage 3 (n = 8)	24.2 ± 9.3	7.9 ± 4.1

SUV standardized uptake value, *SD* standard deviation, *MRONJ* medication-related osteonecrosis of the jaw

Table 4 Patient characteristics and SPECT/CT SUVs of the opposite side of the lesions with medication-related osteonecrosis of the jaw

Patient characteristics	Opposite side of the lesions (Mean ± SD)	
	Maximum SUV	Mean SUV
Age	p = 0.149	p = 0.101
80 years (n = 19)	3.7 ± 1.5	1.5 ± 0.6
≧80 years (n = 20)	4.9 ± 2.6	1.9 ± 0.8
Gender	p = 0.988	p = 0.450
males (n = 11)	4.3 ± 1.9	1.5 ± 0.5
females (n = 28)	4.4 ± 2.3	1.8 ± 0.8
Underlying disease	p = 0.323	p = 0.142
osteoporosis (n = 26)	4.5 ± 2.3	1.9 ± 0.8
bone metastases (n = 13)	4.0 ± 2.1	1.5 ± 0.6
Medication	p = 0.592	p = 0.828
bisphosphonates (n = 25)	4.2 ± 2.1	1.7 ± 0.7
non-bisphosphonates (n = 14)	4.7 ± 2.4	1.8 ± 0.8
Staging of MRONJ	p = 0.173	p = 0.142
stage 1, 2 (n = 31)	4.0 ± 1.9	1.6 ± 0.7
stage 3 (n = 8)	5.7 ± 3.0	2.2 ± 1.0

SUV standardized uptake value, *SD* standard deviation, *MRONJ* medication-related osteonecrosis of the jaw

Table 5 Patient characteristics and SPECT/CT SUVs of the temporomandibular joints with medication-related osteonecrosis of the jaw

Patient characteristics	Right temporomandibular joints (Mean ± SD)	
	Maximum SUV	Mean SUV
Age	p = 0.687	p = 0.945
80 years (n = 19)	2.6 ± 1.1	1.4 ± 0.6
≧80 years (n = 20)	2.5 ± 0.7	1.3 ± 0.3
Gender	p = 0.548	p = 0.177
males (n = 11)	2.5 ± 0.6	1.5 ± 0.5
females (n = 28)	2.5 ± 1.0	1.3 ± 0.5
Underlying disease	p = 0.452	p = 0.713
osteoporosis (n = 26)	2.7 ± 1.0	1.3 ± 0.5
bone metastases (n = 13)	2.3 ± 0.6	1.4 ± 0.5
Medication	p = 0.303	p = 0.228
bisphosphonates (n = 25)	2.5 ± 1.0	1.3 ± 0.5
non-bisphosphonates (n = 14)	2.6 ± 0.8	1.4 ± 0.5
Staging of MRONJ	p = 0.441	p = 0.573
stage 1, 2 (n = 31)	2.5 ± 0.9	1.3 ± 0.5
stage 3 (n = 8)	2.6 ± 0.9	1.4 ± 0.4

SUV standardized uptake value, *SD* standard deviation, *MRONJ* medication-related osteonecrosis of the jaw

Figures

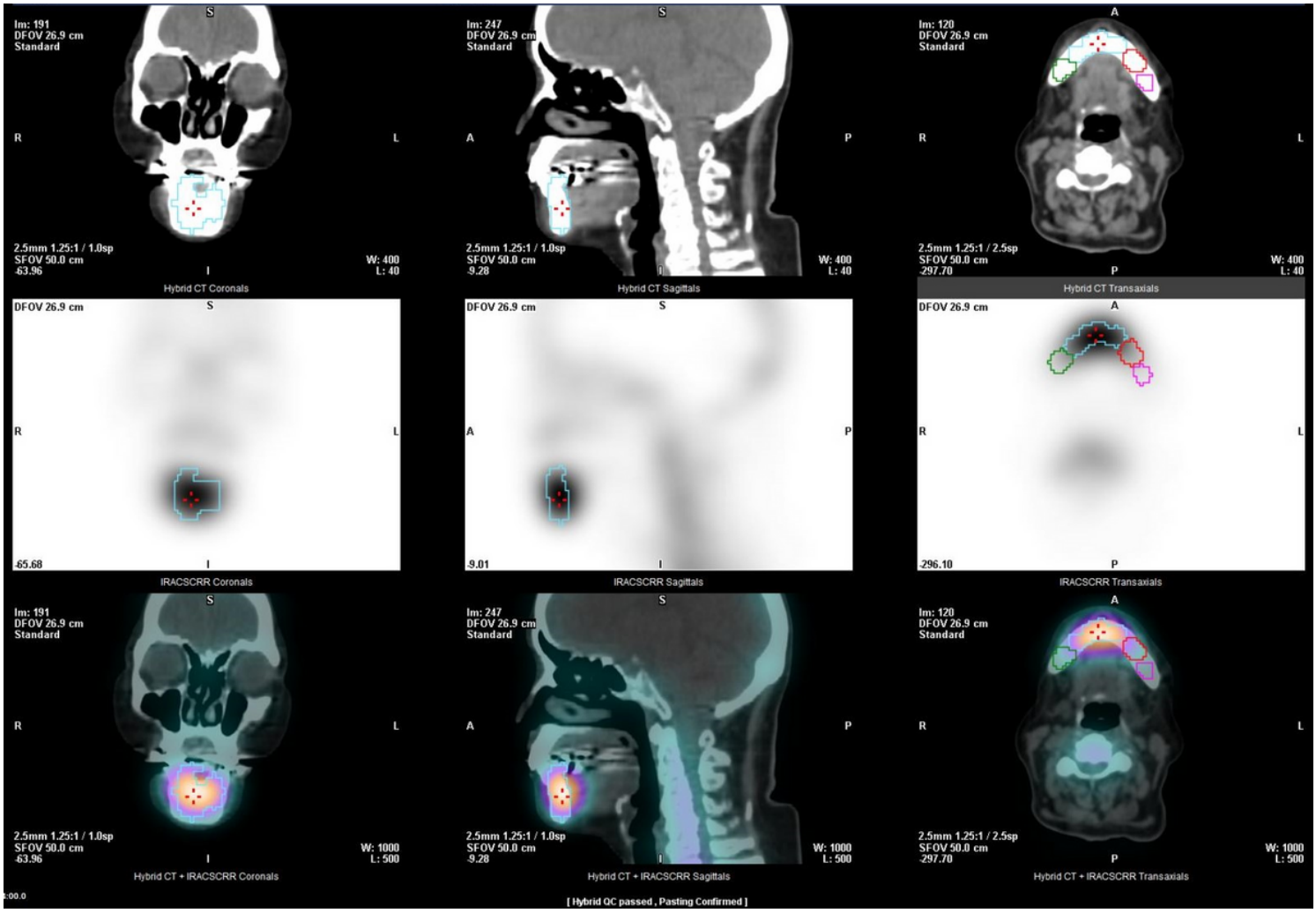
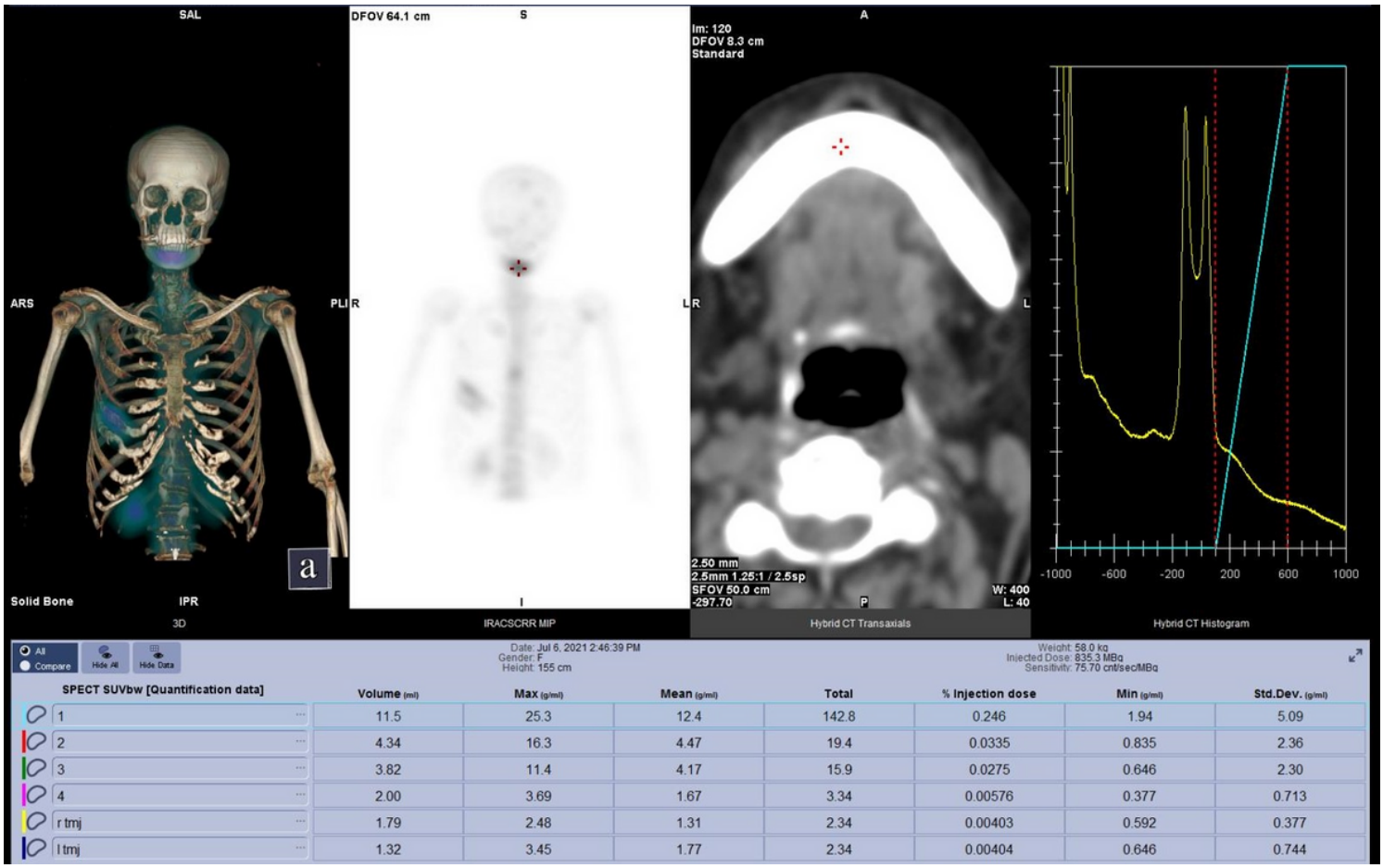


Figure 1

Medication-related osteonecrosis of the jaw of the mandible in a 73-year-old woman with Xeleris 4DR and Q. Volumetrix MI. Using the CT, SPECT and SPECT/CT transaxials, coronals and sagittals as the anatomical reference, the localization and size of volume of interest (VOI) was automatically drawn over the mandibular lesion (sky blue), left (red), right (green), opposite (pink) side of the lesion, right (yellow) and left (blue) temporomandibular joints.



SPECT SUVbw [Quantification data]	Volume (ml)	Max (g/ml)	Mean (g/ml)	Total	% Injection dose	Min (g/ml)	Std.Dev. (g/ml)
1	11.5	25.3	12.4	142.8	0.246	1.94	5.09
2	4.34	16.3	4.47	19.4	0.0335	0.835	2.36
3	3.82	11.4	4.17	15.9	0.0275	0.646	2.30
4	2.00	3.69	1.67	3.34	0.00576	0.377	0.713
r tmj	1.79	2.48	1.31	2.34	0.00403	0.592	0.377
l tmj	1.32	3.45	1.77	2.34	0.00404	0.646	0.744

Figure 2

Medication-related osteonecrosis of the jaw of the mandible in a 73-year-old woman with Xeleris 4DR and Q. Volumetrix MI. Maximum SUVs of the mandibular lesion (sky blue), left (red), right (green), opposite (pink) side of the lesion, right (yellow) and left (blue) temporomandibular joints were 25.3, 16.3, 11.4, 3.69, 2.48 and 3.45, respectively. Furthermore, mean SUVs of the mandibular lesion (sky blue), left (red), right (green), opposite (pink) side of the lesion, right (yellow) and left (blue) temporomandibular joints were 12.4, 4.47, 4.17, 1.67, 1.31 and 1.77, respectively.