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Original article

SPECT/CT localization of oral radioiodine activity: a retrospective study and in-vitro assessment

Jared S. Burlison[a], Michael F. Hartshorne[a], Alan M. Voda[b], Franklin H. Cocks[c] and Joanna R. Fair[a]

Purpose We sought to further localize radioiodine activity in the mouth on post-thyroid cancer therapy imaging using single-photon emission computed tomography/computed tomography (SPECT/CT).

Materials and methods We retrospectively reviewed all patients (58) who underwent thyroid cancer therapy with iodine-131 (^{131}I) at our institution from August 2009 to March 2011 whose post-therapy radioiodine imaging included neck SPECT/CT. A small group (six) of diagnostic ^{123}I scans including SPECT/CT was also reviewed. Separately, we performed in-vitro ^{131}I (sodium iodide) binding assays with amalgam and Argenco HP 77 (77% dental gold alloy) as proof of principle for these interactions.

Results Of the 58 post-therapy patients, 45 (78%) had undergone metallic dental restorations, and of them 41 (91%) demonstrated oral ^{131}I activity localizing preferentially to those restorations. It was observed that radioiodine also localized to other dental restorations and to orthodontic hardware. Gum-line activity in edentulous patients suggests radioiodine interaction with denture adhesive. *In vitro*, dental amalgam and Argenco HP 77 bound ^{131}I in a time-dependent manner over 1–16 days of exposure. Despite subsequent washings with normal saline, significant ^{131}I activity (maximally 12% for amalgam and 68% for Argenco HP 77) was retained by these metals. Subsequent soaking in a saturated solution of potassium iodide partially displaced ^{131}I from amalgam, with near-total displacement of ^{131}I from Argenco HP 77.

Conclusion SPECT/CT shows that radioiodine in the oral cavity localizes to metallic dental restorations. Furthermore, in-vitro studies demonstrate partially reversible binding of ^{131}I to common dental metals. *Nucl Med Commun* 34:1216–1222 © 2013 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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[a]Department of Radiology, University of New Mexico, [b]Private Practice, Albuquerque, New Mexico and [c]Department of Mechanical Engineering and Materials Science, Duke University, Durham, North Carolina, USA

Correspondence to Joanna R. Fair, MD, PhD, Department of Radiology, University of New Mexico, MSC10 5530, Albuquerque, NM 87131-0001, USA
Tel: +1 505 272 2269; fax: +1 505 272 5821;
e-mail: jfair@salud.unm.edu

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Introduction

Single-photon emission computed tomography/computed tomography (SPECT/CT), an indispensable diagnostic tool, provides increased sensitivity for lesion detection, more accurate anatomic localization of radioactive foci, and delineation of pathologic from physiologic uptake [1–5]. Information obtained from SPECT/CT may guide or change the management of patients' disease processes. For thyroid cancer, SPECT/CT for both presurgical planning and radioiodine therapy follow-up yields information not available from traditional planar imaging, which results in more precise staging and thus assists in treatment planning [6,7].

Delineating physiologic from malignant activity is paramount to interpreting radioiodine scans. Unusual sites of nonmalignant radioiodine concentration have been previously identified with traditional planar scintigraphy [8,9]. However, SPECT/CT provides more confident characterization of physiologic activity that may simulate disease. Previous studies used SPECT/CT to document benign radioiodine activity in a variety of locations, ranging from typical (retrosternal goiter) to rare (the menstruating uterus) [10–16].

At our institution, we have performed SPECT/CT (typically of the neck, elsewhere as needed) as part of most postradioiodine therapy scans since 2009. Since doing so, we have anecdotally noted that radioiodine activity localizes to dental restorations (including fillings, crowns, veneers, bridges, implants, and other prosthetic devices). Previous studies suggest that periodontal disease and/or active caries can mimic salivary gland activity [17] and that healing dental sockets (from recent extraction) can cause increased oral radioiodine uptake [18]. However, these studies utilized only planar scintigraphy, limiting precise anatomic localization. To our knowledge, no study has assessed radioiodine localizing specifically to dental restorations.

To further understand this phenomenon, we undertook a retrospective review of all patients over a 2-year period whose post-therapeutic iodine-131 (^{131}I) scans and diagnostic ^{123}I scans included SPECT/CT. Also, as proof of principle, we assessed the interaction between common dental metals and radioiodine *in vitro*.

Materials and methods

Retrospective review

This study was approved by our institutional review board. Whole-body and SPECT/CT post-therapy scans of 58 patients (11 men and 47 women) who received oral ^{131}I sodium iodide for thyroid cancer treatment between August 2009 and March 2011 at the University of New Mexico Hospital were retrospectively analyzed. The average age of the patients was 48.5 years (range 20–76 years). The average administered activity was 5.48 GBq (148 mCi) [range 2.96–7.73 GBq (80–209 mCi)].

Whole-body and SPECT/CT ^{123}I diagnostic scans, performed for follow-up of thyroid cancer patients, were also reviewed from the same time period. These included five patients (one male and four female patients) of an average age of 48.4 years (range 16–63 years). The average administered activity was 171 MBq (4.6 mCi) and ranged from 98 to 200 MBq (2.7–5.4 mCi). One additional diagnostic ^{123}I scan with 14.8 MBq (400 μCi) was acquired with SPECT/CT in a hyperthyroid patient to assess a mediastinal mass.

Before radioiodine administration, thyroid cancer patients were prepared by placing them on a low-iodine diet; they also underwent either thyroid hormone withdrawal (to TSH > 30) or thyrotropin α (Thyrogen; Genzyme Corporation, Cambridge, Massachusetts, USA) injections. Post-therapy ^{131}I scans were performed 6–13 days (average 8.6) after radioiodine administration; diagnostic ^{123}I scans were performed after 1 day. Whole-body planar and SPECT/CT images were obtained with a Siemens Symbia T2 system (Siemens Medical Solutions USA, Malvern, Pennsylvania, USA), with CT images without intravenous contrast in 3 mm sections.

In-vitro ^{131}I binding assays

Dental amalgam samples of 1.15 g (Valiant Ph.D. Sure Cap; Ivoclar Vivadent, Amherst, New York, USA), roughly spherical and measuring about 2.5 mm in radius (surface area of ~80 mm^2), were used. The composition of dental amalgam varies and commonly consists of ~50% mercury, ~25% silver, and smaller amounts of other metals. These amalgam samples were incubated at room temperature in a sealed tube containing a solution of 10 μCi ^{131}I (NaI) diluted in 10 ml of normal saline (NS), with three samples incubated for 1, 8, and 16 days, respectively. ^{131}I was utilized, rather than ^{123}I, because of its much longer physical half-life (enabling longer experiments) and to simulate post-therapeutic imaging. The relatively small amount was arbitrarily selected to approximate small amounts that might be present in the saliva. At our institution, all therapeutic administrations of radioactive iodine are in capsule form; thus, oral radioactive iodine should come only from salivary secretions.

At the end of each incubation, each tube was counted in a Captus 3000 (Capintec Inc., Ramsey, New Jersey, USA) well counter for 1 min and corrected for background activity. The pill was then decanted into another tube, washed with NS for 1 min, and recounted. Washings were repeated until the change in remaining activity after washing was less than the background activity. The percentage of retained activity was then calculated as follows: (activity remaining after washings) × 100/(initial activity in the tube before washings). Subsequently, these amalgam pills were soaked in 10 ml of supersaturated solution of ^{127}I [saturated solution of potassium iodide (SSKI)] for 1 day (for the 1-day ^{131}I soak) or for 3 days (for the 8- and 16-day ^{131}I soaks) in a sealed tube. Similar NS washing cycles were repeated to determine the remaining ^{131}I activity after the SSKI soak.

Similarly, ^{131}I uptake was assayed on a sample of dental gold: standard pennyweight (1.9 g) dental gold alloy Argenco HP 77 (77% gold, 13% silver, 8.55% copper, 1.0% platinum, and <1% each of iridium, indium, and zinc). Each sample measured 13 × 8 × 1 mm (surface area of ~250 mm^2). Similar experiments on the dental amalgam were performed with this alloy, with the same alloy sample being used each time, and then decayed to background before the next experiment. Experiments performed were a 1-day ^{131}I incubation [10 μCi ^{131}I (Na) in 10 ml NS] followed by a 3-day SSKI soak, a 7-day ^{131}I incubation with a 1-day SSKI soak, and a 14-day ^{131}I incubation with a 3-day SSKI soak.

Results

Retrospective review

Of the 58 post-therapy patients imaged, 45 (78%) showed metallic dental restorations on CT, typically with a beam hardening artifact, and of them 41 (91%) demonstrated oral ^{131}I activity localized to the restorations. In patients with bilateral restorations, activity was typically bilateral (Fig. 1a and b), although sometimes asymmetric (Fig. 1c and d). In patients with unilateral metallic dental restorations, the ^{131}I activity typically localized to that side. Similar to ^{131}I, ^{123}I localized to metallic dental restorations when present (not shown). Radioiodine (^{131}I and ^{123}I) also localized to other metallic appliances such as braces, palate expanders, and tongue piercings (Fig. 1e and f, and additional data not shown). As alluded to above, four patients with metallic dental restorations did not demonstrate localizing oral radioiodine activity. In our study, which is a retrospective review, the compositions of the patient's restorations are unknown. It is possible that some dental metals are not radioiodine avid, a hypothesis that could be tested but is beyond the scope of this study.

Three patients without any metallic dental restorations or evidence of prior dental procedures showed mild, diffuse, nonlocalizing oral cavity activity (Fig. 1g and h). In contrast to the metallic restorations typically seen in our patient population, one patient had molar restorations without significant beam hardening artifacts (Fig. 1i and j), presumably nonmetallic. Interestingly, radioiodine activity in this patient did not localize to the restorations; instead, the low-level, diffuse oral mucosal activity was similar to that seen in patients without metallic dental restorations or appliances. This suggests that radioiodine interacts directly with dental metals rather than simply penetrating into crevices or other nonanatomic spaces.

In total, 11 patients from the ^{131}I group had localizing oral radioactivity not corresponding to metallic dental restorations. Of them, three edentulous patients had radioiodine activity concentrated along the gum lines (Fig. 2), suggesting that radioiodine adheres to or interacts with residual denture adhesive. Three near-edentulous patients had ^{131}I activity localizing to the remaining teeth. Interestingly, one such near-edentulous patient with ^{131}I activity localizing to the remaining teeth (Fig. 3, eight teeth, no hardware) also accumulated activity on his scalp and hands, suggesting that poor hygiene may have contributed to dental ^{131}I activity. In the remaining five patients with localizing activity, ^{131}I nonspecifically associated with unrestored teeth.

In-vitro ^{131}I binding assays

For a proof-of-principle assessment of radioiodine binding to dental metals, we performed in-vitro binding assays with samples of dental amalgam and Argenco HP 77 incubated with an ^{131}I/NS solution for varying time periods, followed by multiple washings (Fig. 4). After washings, typical ^{131}I activities ranged from 5×10^6 to 5×10^4 cpm, whereas the daily measured background was 150–180 cpm

For dental amalgam samples (Fig. 5), binding increased with increasing incubation time. After 1, 8, and 16 days of incubation, 1.5, 3.4, and 12%, respectively, remained. Subsequent soaking with SSKI for 1–3 days (followed by NS washes) partially displaced the ^{131}I, with the maximum displacement being $\sim$30%. Accordingly, a relatively strong physical interaction and/or chemical binding of radioiodine to dental amalgam must be present.

For the Argenco HP 77 gold alloy (Fig. 6), binding likewise increased with increasing incubation time: only

Fig. 1

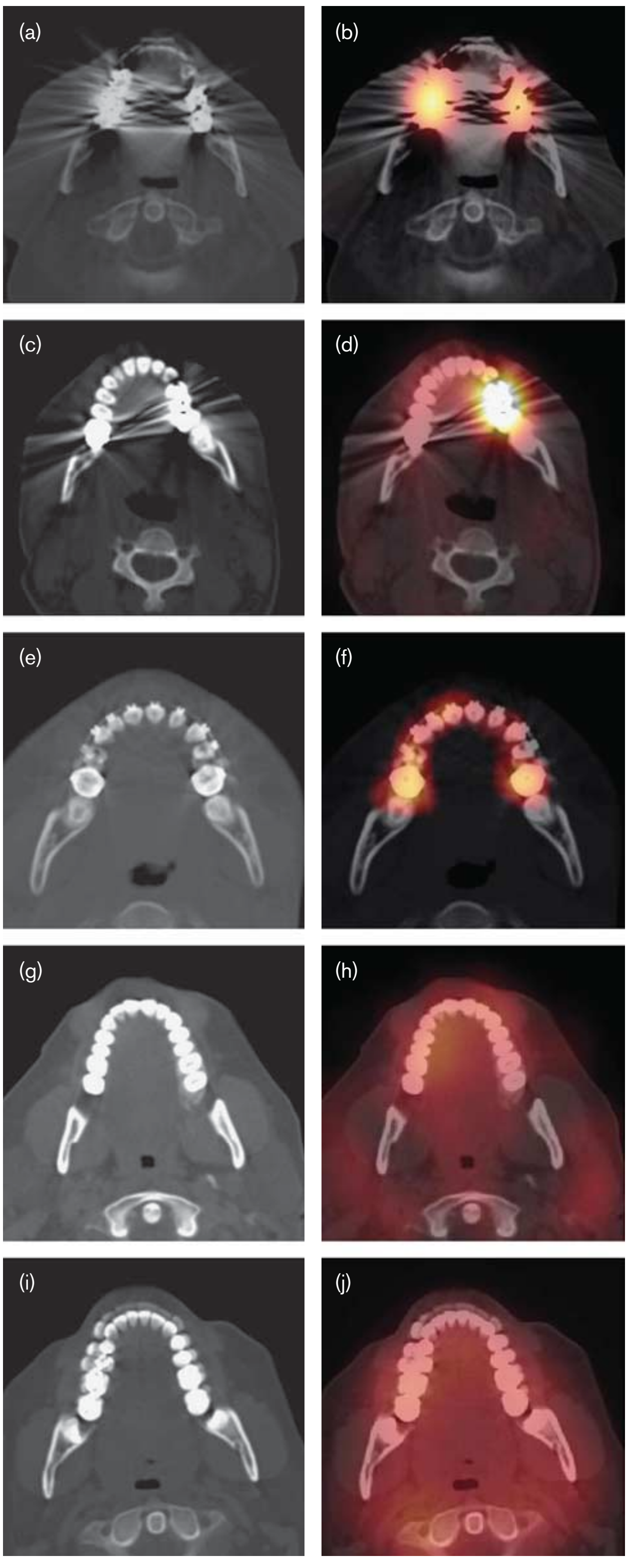
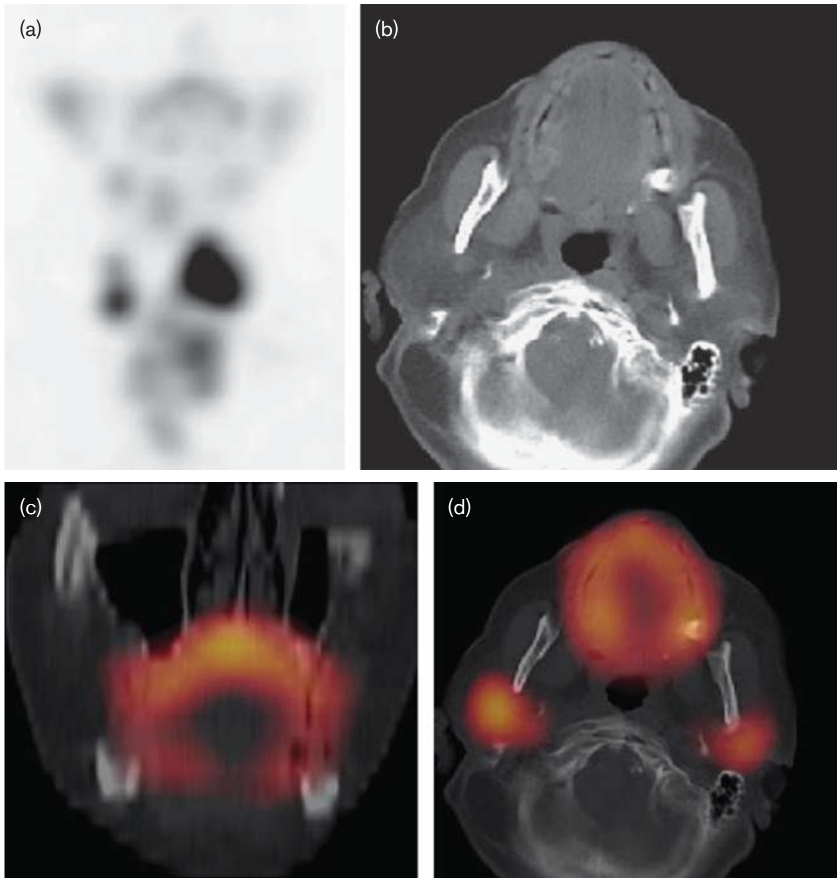


Fig. 1

Post-therapeutic SPECT/CTs of the neck showing ^{131}I localizing to metallic dental restorations. The left column contains axial CT images through the oral cavity; the right column contains the corresponding axial SPECT/CT fused images. (a, b) Bilateral beam hardening artifact associates with bilateral molar metallic dental restorations, localizing symmetric radioiodine activity. (c, d) Bilateral metallic beam hardening artifact associates with bilateral mandibular dental restorations, greater on the left, with asymmetric (left greater than right) radioiodine localization. (e, f) Metallic orthodontic appliances localizing radioiodine activity, most intensely to circumferential metallic molar bands. (g, h) No metallic dental restorations or evidence of prior dental procedures, with nonlocalizing, low-level oral radioiodine uptake. (i, j) Molar restorations without metallic beam hardening artifact demonstrate nonlocalizing, low-level oral radioiodine uptake. SPECT/CT, single-photon emission computed tomography/computed tomography.

Fig. 2



Diagnostic ^{123}I SPECT/CT of the neck and upper chest to assess a mediastinal mass (confirmed to be a multinodular goiter) shows gum-line activity in this edentulous patient, presumably bound to denture adhesive. (a) The MIP (maximal intensity projection) shows multiple foci of activity associated with the multinodular goiter, along with physiologic submandibular gland activity and curvilinear activity in the mouth. (b) The CT image through the mouth shows that the patient is edentulous. Coronal (c) and axial (d) SPECT/CT fusion images demonstrate radioiodine activity localizing along the gum lines. SPECT/CT, single-photon emission computed tomography/computed tomography.

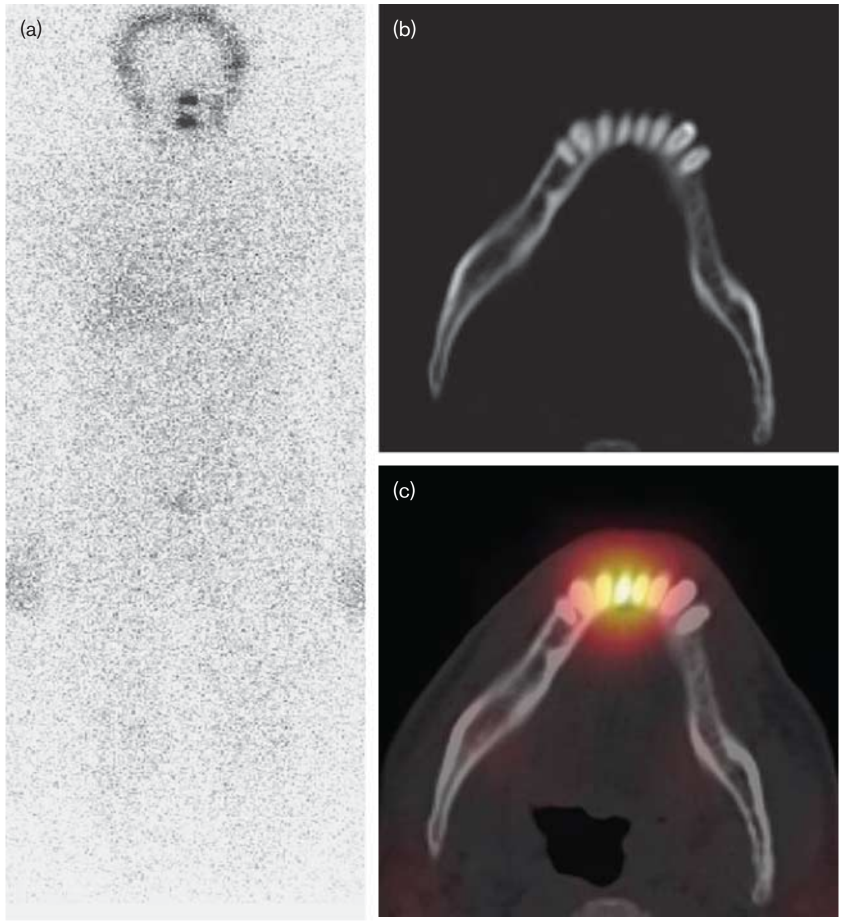
1.4% of the ^{131}I bound after 1 day, in contrast with 51 and 68% after 7 and 14 days, respectively. Even with a 2-day shorter incubation compared with the amalgam 16-day incubation samples, significantly more radioiodine bound to the Argenco HP 77 at 14 days, which was confirmed with repeated incubations. For the 1-day incubation, 3 days in SSKI displaced an additional 28% of ^{131}I from Argenco HP 77, whereas only 1 day of SSKI soaking displaced nearly all of the remaining ^{131}I bound to the 7- and 14-day samples. Presumably, the relatively small amount removed from the 1-day ^{131}I incubation by the 3-day SSKI soak is attributable to the very little ^{131}I (1.4%) that remained on the sample after NS washes.

Discussion

Although oral radioiodine activity has been routinely observed on whole-body planar radioiodine imaging, this study more specifically characterizes this nonpathologic finding. Our SPECT/CT images qualitatively demonstrate that oral radioiodine activity typically localizes to metallic dental restorations when present. Individuals without metallic dental restorations or other oral metallic appliances typically did not demonstrate localizing oral activity; instead, diffuse, low-level oral radioiodine activity likely reflects physiological mucosal activity or glandular secretions.

Two plausible explanations for this radioiodine localization are as follows: either metallic dental restorations themselves bind radioiodine, or radioiodine penetrates into crevices or irregular interfaces between dental restorations and enamel. Of note, the one patient we reviewed with nonmetallic dental restorations had no oral radioiodine activity localizing to the restorations. This suggests that radioiodine directly interacts, at least in part, with metallic dental restorations. The observation that radioiodine localizes to other oral metallic appliances such as orthodontic braces supports a direct iodine–metal interaction. However, not all dental metals localize radioiodine equally, concordant with the in-vitro results discussed below.

Fig. 3

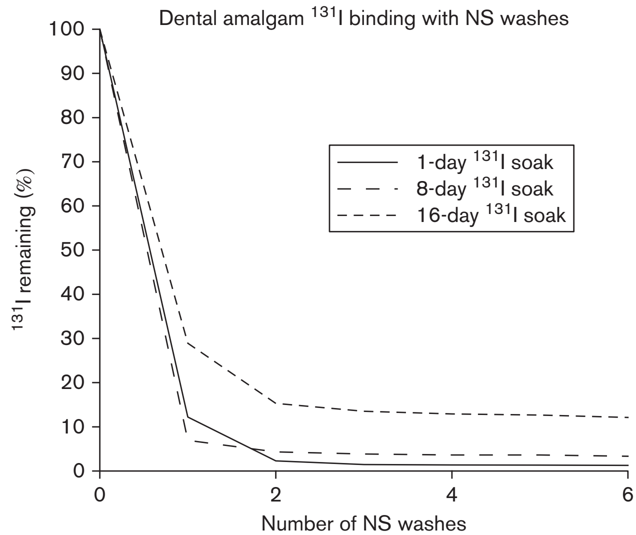


Post-therapeutic whole-body planar iodine-131 (^{131}I) images with neck SPECT/CT showing poor hygiene (hand/scalp activity) and activity localizing to the remaining teeth, possibly also attributable to poor hygiene. (a) Anterior image from whole-body planar imaging demonstrates ^{131}I activity along the scalp and hands, as well as in the nose and mouth. (b) The CT image through the mouth shows that the patient has only eight remaining mandibular teeth. (c) The corresponding axial SPECT/CT fusion image demonstrates intense activity localized to these unrestored mandibular teeth. SPECT/CT, single-photon emission computed tomography/computed tomography.

Oral radioiodine showed focal localization in some patients without metallic dental restorations or oral hardware. Gum-line radioiodine activity in denture wearers was presumably bound to dental adhesive. Patients with poor dentition showed intense localization to the remaining teeth, for which a few explanations are plausible. First, it has been shown (on planar scintigraphy) that radioiodine activity can associate with periodontal disease, active caries, or recent dental extractions [17,18]. Second, enamel defects in the teeth of patients with poor dentition could allow radioiodine to penetrate and bind. Third, these patients may have brushed their teeth infrequently; calcified plaque matrix buildup could provide a more radioiodine-avid surface.

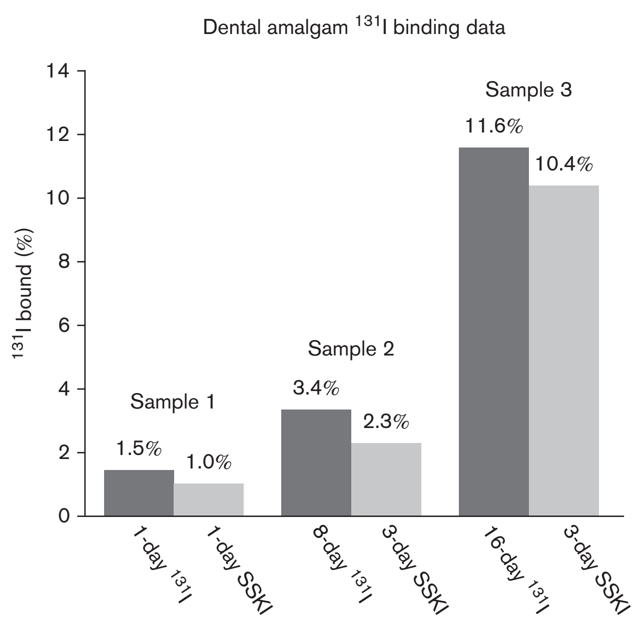
As proof of principle for our hypothesis that radioiodine can interact with metallic dental restorations, in-vitro binding assays demonstrate partially reversible binding of ^{131}I to dental amalgam and Argenco HP 77. A significant portion of radioiodine remained bound despite NS washes, suggesting that saliva alone would not remove all radioiodine bound to existing dental restorations *in vivo*. Our results also demonstrate a time-dependent increase in ^{131}I uptake on dental amalgam and Argenco HP 77. Similarly, the in-vitro experiments showed differences in ^{131}I binding between dental amalgam and Argenco HP 77, similar to our observation that metallic dental restorations *in vivo* demonstrate differential radioiodine avidity. The difference between maximal ^{131}I binding to amalgam versus Argenco HP 77 (12 vs. 68%) may partly be due to differences in composition (discussed further below) as well as due to the three-fold greater surface area of the Argenco HP 77 sample. The scope of this study did not encompass all dental restorative materials: it remains possible that some dental metals are not radioiodine avid, a testable hypothesis that could explain why a small percentage of patients with metallic dental restorations do not demonstrate localizing oral radioiodine activity.

Fig. 4



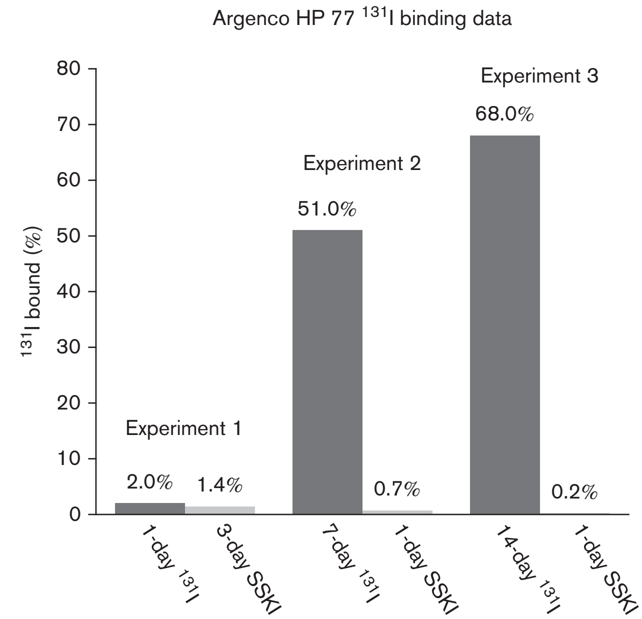
Percentage of initial radioiodine retained in dental amalgam samples after multiple normal saline (NS) washes, with non-zero asymptotes indicating residual iodine-131 (^{131}I) binding. Washes were continued until the change in radioiodine activity remaining after the final wash was less than background activity. This washing procedure was performed for all dental metal samples, both after the ^{131}I/NS incubation and after the saturated solution of potassium iodide soak.

Fig. 5



Percentage of iodine-131 (^{131}I) retained in dental amalgam samples after incubating in ^{131}I/normal saline (NS) solution and subsequent saturated solution of potassium iodide (SSKI) soak (each after multiple NS washes). The greatest radioiodine retention occurs with the longest ^{131}I/NS incubation time, and most of the initially bound radioiodine is retained after SSKI soaking.

Fig. 6



Percentage of iodine-131 (^{131}I) retained in Argenco HP 77 after incubating in ^{131}I/normal saline (NS) solution and subsequent saturated solution of potassium iodide (SSKI) soak (each after multiple NS washes). The greatest amount of radioiodine retention occurs with the longest ^{131}I/NS incubation time. Except for the 1-day ^{131}I/NS incubation, with very little ^{131}I retained, most radioiodine is removed by the SSKI soak.

The binding and subsequent removal of ^{131}I from dental materials can likely be explained by a combination of several processes. ^{131}I likely both adsorbs and chemisorbs onto all of these materials, in varying degrees. In addition, ^{131}I is likely absorbed into the corrosion product films that form on these materials under corrosive conditions, including saliva and salt solutions.

Electrochemical corrosion rate measurements *in vivo* with adult male *Papio anubis* baboons have shown that the corrosion rate of amalgam is far higher than that of gold. In addition, the corrosion rate of both materials decreases as corrosion product films develop, if not removed, for example, by abrasive processes [19]. The corrosion films, not totally impervious, should physically absorb ^{131}I. The film surfaces and uncorroded metal should also chemisorb and adsorb ^{131}I. Chemisorbed ^{131}I would be relatively tightly bound by varying covalent-like bonds, whereas adsorbed layers formed over chemisorbed layers are more loosely bound by van der Waals forces. SSKI soaking might displace absorbed and adsorbed ^{131}I from the corrosion product film that forms on amalgam, but not to the same extent as chemisorbed ^{131}I. This chemisorbed ^{131}I may account for the remaining radioiodine activity on the dental amalgam after washing and SSKI soaking.

Corrosion product films are of varying porosity, depending on the base alloy and the corrosive environment.

The osmotic differences between the fluid entrained in the film and the washing and soaking fluids can contribute to ^{131}I removal, and the osmotic pressure induced by SSKI will far exceed that of NS or the ^{131}I solution because of the higher salt concentration in SSKI.

As noted above, gold alloys corrode at a substantially slower rate compared with amalgam, and, for a given exposure time, the corrosion product films on gold alloys will be thinner and less complete [19]. Thus, the corrosion product films on Argenco HP 77 in our experiments are presumably very thin, but will increase with increasing exposure time. It is not surprising that more ^{131}I is retained by the Argenco HP 77 after the 14-day incubation than after the 1-day incubation, as the corrosion product film after 14 days would be more substantial.

Very little ^{131}I remains on the Argenco HP 77 after the SSKI soak in all experiments; however, a greater amount is retained after the 1-day ^{131}I/NS incubation than after the 14-day incubation. The 1-day incubation should produce a smaller amount of corrosion product film compared with the 14-day incubation. Thus, the greater amount of ^{131}I retained in this case may be attributable to the greater average bond strength of ^{131}I chemisorbed onto the gold alloy surface itself than onto the corrosion product film.

Of note, our proof-of-principle in-vitro experiments clearly do not directly simulate the complex environment in the mouth, where a variety of chemical (foods/liquids) and mechanical (brushing) interactions take place. For example, in-vitro tests in synthetic saliva have shown that corrosion rates of dental alloys will substantially increase if the corroding sample is exposed to ultrasonic vibration in synthetic saliva containing silicon carbide grit, a process that erodes corrosion product films [20]. Thus, mechanical brushing likely alters ^{131}I binding to dental metals and their corrosion product films. NS is also not directly equivalent to saliva, and proteins in saliva likely bind secreted radioiodine. Nevertheless, our in-vitro studies provide a first approximation for explaining our SPECT/CT findings. Future studies could assess mechanical removal (e.g. brushing) of radioiodine from fillings.

Conclusion

Post-therapeutic ^{131}I and diagnostic ^{123}I SPECT/CT scans demonstrate radioiodine activity localizing to metallic dental restorations and to other dental appliances. In addition, gum-line localization and activity along the remaining teeth were observed in edentulous and near-edentulous patients. Supporting our hypothesis that ^{131}I interacts with metallic dental restorations, proof-of-principle in-vitro radioiodine binding assays demonstrate partially reversible binding to dental amalgam and Argenco HP 77, with a significant amount remaining bound to these metals despite NS washing.

Acknowledgements

Conflicts of interest

Dr Fair has served as a consultant to Lilly/Avid Radiopharmaceuticals and has received an educational grant from Cardinal Health, both for work unrelated to the current study. For the remaining authors there are no conflicts of interest.

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