Lymphoscintigraphy in Melanoma: Initial Evaluation of a Low Protein Dose Monoclonal Antibody Cocktail

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Abstract

A low protein dose (73 ± 10 µg total) 131I-labeled monoclonal antibody cocktail made of equal µg quantities of 225.28S (IgG2a) and 763.24T (IgG1) murine monoclonal antibodies, which bind additively to a high molecular weight antigen of melanoma, was evaluated as a lymphoscintigraphic agent in 17 patients with intermediate to thick (mean Breslow depth, 3.39 ± 0.64 mm) melanomas or clinical Stage II disease scheduled for nodal dissection. Eleven of the patients were clinically Stage I while 6 were clinically Stage II. 131I antibody cocktail, 258 ± 10 µCi, was administered s.c. at the site of the primary melanoma or its scar following surgical removal. In eight patients, 63 ± 8 µCi of 131I nonspecific normal sheep IgG was coadministered s.c. Gamma camera imaging was conducted beginning immediately after and continuing for several days following injection. Surgical resection, weighing, and gamma counting of the draining lymph nodes were undertaken in all patients. On gamma scans, early nodal uptake of antibody was most pronounced and of longest duration in the tumor pathologically positive patients (5 of 7 had visible nodal uptake, 4 of 7 visually stable or rising with time), with the tα, of nodal clearance by gamma scan significantly (P < 0.05) longer than in the negative patients in whom 4 of 10 showed some, although generally transient (0 of 10 stable or rising), nodal uptake. Scans were not easily interpretable when the injection site was very near the draining nodal group, in part due to the detection of scatter activity from the injection site. In several instances the scan was correct and the clinical examination was incorrect as regards nodal disease. Quantitative analysis of the surgically excised draining nodes showed significantly (P < 0.001) more 131I anti-melanoma antibody uptake in the 21 tumor-involved nodes [0.01217% injected dose (ID)/node median] than in the 512 tumor-negative nodes (0.00051% ID/nodule median). Median percentage ID/g of anti-melanoma antibody in tumor-involved nodes was significantly greater (P < 0.01) than in tumor-negative nodes (0.01984 versus 0.003215% ID/g). Median percentage ID/nodes of anti-melanoma antibody in tumor-involved nodes was significantly greater (P < 0.01) than in tumor-negative nodes (0.01984 versus 0.003215% ID/g). These data demonstrate that by external imaging and by tissue counting a radionuclide anti-melanoma monoclonal antibody cocktail can specifically accumulate to melanoma-involved lymph nodes following s.c. administration. While these results are promising and demonstrate the feasibility of the method, additional clinical study of this low protein antibody cocktail approach will be necessary to more fully evaluate the utility of the technique for the evaluation of nodal involvement in melanoma.

Introduction

The optimal approach to the management of draining lymph nodes in clinical Stage I melanoma is controversial (1). While some studies have shown no improvement in survival if regional draining lymph nodes are removed, others strongly suggest that there is a significant survival benefit for patients with Stage I melanomas of intermediate thickness, between 1.7 and 4 mm, if their draining lymph nodes are removed surgically shortly after the diagnosis of cutaneous melanoma (2–4). Presumably the survival benefit is due to the surgical removal of lymph nodes that contain small foci of melanoma prior to more generalized dissemination. There is certainly no disagreement that surgery is the appropriate treatment for Stage II melanoma, although occasionally clinically enlarged draining lymph nodes do not harbor tumor. Clearly, a method capable of separating those patients with lymph node metastases from those without such involvement would be extremely valuable preoperatively, particularly since currently the majority of patients operated upon in a prophylactic setting do not have nodal involvement with tumor (1).

While selecting the lymph node groups at risk for metastases in patients with melanoma can be achieved by the s.c. injection of radiolabeled albumin or colloid about the primary tumor or its scar (lymphoscintigraphy) with sequential gamma imaging, this approach only tells of potential draining lymph nodes and does not reveal whether they are involved with tumor (5, 6). In the past several years, attempts have been made to use radiolabeled monoclonal antibodies to image melanoma and a variety of other tumors following i.v. antibody administration (7–9). These approaches have shown promise in that a variety of visceral foci of metastases have been detected following i.v. administration. These studies using the i.v. administration of antibody have generally been limited by high background activity and low absolute radioantibody uptake in tumor foci. One approach to enhancing tumor uptake of monoclonal antibodies is to administer the agents by the s.c. or i.l. route, where there would be preferential uptake by lymph nodes (10–12). The antibody lymphoscintigraphy approach appears promising in several diseases, but to date attempts to use this seemingly rational technique for the detection of melanoma nodal metastases have been disappointing due to high background nodal activity and/or low target uptake (13–18).

The previous reports of antibody lymphoscintigraphy in melanoma have used single anti-melanoma antibodies or fragments and have in many cases imaged only for a relatively short time following s.c. injection (16–18). In this communication we report our clinical experience with antibody lymphoscintigraphy in patients with cutaneous melanoma scheduled for surgery. A monoclonal antibody cocktail of 2 antibodies reactive with different epitopes of the same high molecular weight antigen of melanoma and thus capable of additive binding was used (19). Since there is a clear dose dependence of lymph node uptake of s.c. administered antibody in experimental models and humans, and apparently considerable first pass extraction by lymph nodes, it is possible that antibody excess may be achieved at the tumor-involved node when antibodies are given s.c. and that unbound antibody may overflow systemically and raise background activity (15, 20, 21) Fig. 1A). For this reason an antibody cocktail, where each antibody is given at a low protein dose,
Materials and Methods

Antibodies. 763.24T is an IgG1 murine monoclonal antibody reactive with a high molecular weight chondroitin sulfate proteoglycan antigen present on the surface of >90% of melanomas and few normal cells (19). It was grown as ascites in BALB/c mice and purified from ascites by 50% ammonium sulfate precipitation and DEAE anion exchange chromatography (Whatman) (21). 225.28S is an IgG2a murine monoclonal antibody reactive with the same antigen, but binds to a different epitope (19). It was also grown in BALB/c mice as ascites and purified by staphylococcal protein A chromatography (23). The antibody cocktail was formed by combining equal protein masses of each antibody. The preparations are free of murine viral, mycoplasmal, bacterial, and endotoxin contamination. Normal sheep IgG was collected by phlebotomizing a healthy sheep, 50% ammonium sulfate precipitation of the plasma, and DEAE chromatography. This preparation was also sterile and pyrogen free. All antibodies were >90% pure by sodium dodecyl sulfate-polyacrylamide gel electrophoresis gels (24). Radiolabeling with I125 or I131 was conducted using the Iodobead (Pierce) method, with separation of free from protein bound iodine by sizing chromatography (BioGel P-60). More than 90% protein bound iodine in the injected product was demonstrated by silica gel thin layer chromatography. Immunoreactivity using this labeling approach was >40% when assayed under conditions approaching antigen excess (HTB63 melanoma target cells; ATCC, Bethesda, MD) (25). Average I125 specific activity was 3.5 µCi/µg. Average I131 specific activity was 2.1 µCi/µg. The antibodies were prepared under the guidelines of a physician-sponsored new drug investigation.

Patients. Seventeen patients with clinical Stage 1 (N = 10) or II (N = 7) melanoma who were scheduled for lymph node dissections were studied using the antibody cocktail after informed consent was obtained (Table 1). All patients were recruited from the multidisciplinary melanoma clinic at the University of Michigan. The median Breslow thickness of the primary lesions was 2.5 mm, and the median age was 65 years. All patients had good functional status and no evidence for visceral metastases at the time of study, based on staging blood tests, physical examinations, chest radiographs, and computer-assisted tomographic scans if indicated. All studies were conducted with subjects as inpatients at the Clinical Research Center. A complete history and physical examination were obtained at admission with particular attention to the clinical stage of the melanoma.

Antibody Injection and Imaging. After written informed consent was obtained, the patients were begun on SSKI, drop p.o. 3 times a day, to block thyroidal iodine uptake prior to injection and were maintained on this for 10 days. A 258 ± 10 (SD) µCi (73 ± 10 Mg) dose of the I131 monoclonal antibody cocktail was injected p.l. about the perimeter of the dermis (26). Injections were completed in 10 min or less. In 8 patients, I125 sheep IgG was also included in the injection mixture (63 ± 8 µCi; 31 ± 21 µg). Vital signs were monitored frequently pre- and postinjection. Blood, urine, and fecal samples were obtained sequentially until the patients went to surgery. Gamma camera imaging was initiated immediately following injection, using a large field of view gamma camera and high energy collimator, with simultaneous analog and digital computer data acquisition. Spot views of the injection site and draining nodal region of 5–20 min duration were obtained centered on the I131 photoprobe ±20%. Sequential images were obtained at frequent intervals during the first day and then daily until surgery, with repositioning achieved through the use of anatomic markers. If draining nodal groups were imaged near the injection site, lead shielding was placed over the injection site to diminish the imaging of scattered activity. Serial changes in regions of interest (injection site or nodes) were determined by manually drawing on the computer a constant size region of interest over the relevant nodal region with values expressed as decay corrected counts/region of interest and plotted. Determination of clearance from regions was through use of a commercial pharmacokinetics software package (R-STRIP; Micromath, Inc., Salt Lake City, UT). A composite interpretation of gamma images was generated by two experienced observers (one without knowledge of patient history or physical examination) and detailed whether and to what extent lymph nodes were visualized as well as the degree of nodal persistence of activity.
The median time to surgery from radioantibody injection was 72 h. At embedding media) and examined histologically, with a diagnosis of surgical resection of the lymph nodes in the draining nodal basin(s).

Antigen is formalin labile) were examined immunohistochemically separately using the intact 225 or 763 antibodies and the avidin/biotin/peroxidase approach (26). Multiple tumor-negative nodes were similarly analyzed. The percentage of injected dose/g was calculated using appropriate corrections for decay or isotope spillover if a dual-label study was performed (27). Contact autoradiography of frozen sections of nodes using Kodak XAR film was also conducted, when possible, on tumor-positive and tumor-negative sections from nodes that contained sufficient counts to predict successful film exposure.

Statistical testing was performed after the uptake data or nodal weights were logarithmically transformed, inasmuch as the variance of the tumor positive nodes was greater than that of the tumor-negative nodes. Then the average of activity was calculated for the positive or negative nodes per individual. The difference of the two averages was then divided by the square root of the variance (SD) to form the t statistic. The t statistic under heterogeneity is thus reported. A nonparametric test was also used to compare the tumor-positive to the tumor-negative nodes across the entire population. The lack of significant difference in pathologically negative node size between tumor-negative and tumor-positive patients was shown using the Behrens-Fisher two-sample t test.

Results

In Vitro

The separate components of the 763/225 mixture do not cross-block significantly in the HTB 63 melanoma system. Both the 763 and 225 antibodies are required to achieve total blocking of the antibody cocktail (Fig. 2).

Toxicity

The immunolymphoscintigraphy was extremely well tolerated with only minimal discomfort due to the local injections of antibody. In one patient a transient low grade fever to 37°C was seen 12 h following injection which rapidly responded to antipyretics. No hematological, renal, or hepatic toxicities were noted on follow-up blood profiles. No patients complained of arthralgias, or rash, to suggest the development of serum sickness.

Imaging

Injection Site Clearance. The disappearance of antibody from the injection site was relatively slow, as is shown in Fig. 3. The mean t<sub>50</sub> of clearance was 33.4 ± 5.9 h.

Regional Lymph Node Imaging. The uptake of antibody in regional lymph nodes ranged from intense and prolonged with strikingly little background activity (Fig. 4) in a lymph node tumor-positive patient (Patient MT; imaged at 19 and 41 h) to absent (20-min and 23-h images; Patient BM) in the majority of tumor-negative lymph node patients (Fig. 5). Of note is that the patients in Figs. 4 and 5 had their primary tumors in the lower extremities but had markedly different uptake patterns in the inguinal and femoral nodal draining groups. By visual interpretation of the scans, 5 of 7 of the patients with pathologically proven lymph node involvement had visualization of draining lymph nodes seen on the scan of which 4 were visible on later images. In 6 of the 10 patients without nodal tumor no lymph node uptake was seen (Table 2). Nodal visualization was, however, also seen in 4 of 10 patients without tumor pathologically. In this pattern, there was early but generally transient
uptake of radioactivity in a draining lymph node following injection, which commonly faded relatively rapidly (Fig. 6, 1 and 29 h; Patient OG). Also apparent in several instances was the injection site activity, despite covering the injection site with lead (Patient PH) (Fig. 7). This is due to inability to shield the high energy γ-rays of $^{131}$I. This inability to totally shield the injection site makes it difficult to image draining lymph nodes located very near the injection site. This is of greatest practical importance in head and neck melanomas where the primary lesion is often very near the draining nodes and in which the scatter from the injection site degrades the image. Of note is that our two false negative scans occurred in this setting. Thus, the technique does not appear to be useful, in our limited experience, when the injection site is so near the draining nodes that the $^{131}$I activity degrades the nodal image. Fig. 7 in node-negative Patient PH demonstrates an intermediate scan pattern in which there is (a) intense immediate uptake in the both axilla, right greater than left (Fig. 7A); with a somewhat less rapid drop in right axillary activity seen on 6.5- and 24-h images (Fig. 7, B, and C).

The uptake and relative retention of radiolabeled antibody in the lymph nodes as visually assessed are illustrated in Table 2. Note that both the tumor-positive patients and some of the tumor-negative patients have initial radiolabeled antibody uptake, but the tumor-positive patients tend to have more prolonged nodal uptake. Thus, if the visual assessment of “positivity” is based on delayed nodal uptake being visibly equal to or more than initial uptake, 4 of 7 tumor-positive patients and 0 of 10 tumor-negative patients have the finding ($P = 0.006$).

This subjective assessment of duration of nodal uptake on scans can also be addressed on gamma scans in which quantitative analysis of the regions of interest drawn over the lymph node groups of the tumor-positive and tumor-negative patients is undertaken. The results of this analysis are shown in Fig. 8 and Table 2. Note that the $t_o$ in the tumor-positive patients was significantly ($P < 0.05$) higher than in the tumor-negative patients (if determinable). Fig. 8 suggests that at later time points tumor involved nodes may be separable from tumor uninvolved by their nodal counts in many cases, corresponding well with our visual assessment.

Of particular interest was that while 10 of our patients were clinically Stage I in disease and 7 were clinically Stage II, the
Fig. 5. Anterior images of the pelvis of Patient BM acquired 20 min (A) and 23 h (B) after radioantibody injection into the p.l. skin of the right thigh. Nodal activity is absent in this patient, whose nodes did not contain melanoma at surgery. Scatter activity from the injection site is seen in the lower aspect of the image. A radioactive marker (M) on the right iliac crest and small amount of bladder activity (arrow) are seen in B.

Table 2. Scintigraphic and histological results

<table>
<thead>
<tr>
<th>Patient</th>
<th>Early scan</th>
<th>Late scan</th>
<th>Nodal pathology</th>
<th>H from injection to surgery</th>
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<tbody>
<tr>
<td>S.BAN</td>
<td>_</td>
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<td>ND</td>
</tr>
<tr>
<td>JK</td>
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<tr>
<td>OG</td>
<td>++</td>
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<td>14.5</td>
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<tr>
<td>PH</td>
<td>++</td>
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<tr>
<td>BK</td>
<td>_</td>
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<td>_</td>
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<td>ND</td>
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<tr>
<td>WW</td>
<td>++</td>
<td>_</td>
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<td>4.72, 7.07</td>
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<tr>
<td>VH</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>ND</td>
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<tr>
<td>S.BAR</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>ND</td>
</tr>
<tr>
<td>MB</td>
<td>_</td>
<td>+</td>
<td>+</td>
<td>Positive</td>
</tr>
<tr>
<td>S.BEA</td>
<td>_</td>
<td>_</td>
<td>_</td>
<td>ND</td>
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<tr>
<td>WP</td>
<td>_</td>
<td>+</td>
<td>+</td>
<td>Positive</td>
</tr>
<tr>
<td>MT</td>
<td>++</td>
<td>_</td>
<td>_</td>
<td>52.2, 102.6</td>
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<tr>
<td>LP</td>
<td>_</td>
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<td>ND</td>
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<td>WT</td>
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<tr>
<td>RU</td>
<td>++</td>
<td>++</td>
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<td>2493 h</td>
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¹ =, no apparent uptake; +, uptake slightly greater than background; ++, uptake distinctly greater than background; ND, not determined.

* Image degraded by scatter from injection site.

scan, using the quantitative technique, correctly indicated tumor involvement in one of the clinical Stage I patients subsequently shown to have tumor and correctly indicated the lack of tumor

Fig. 6. Posterior images of the upper chest of patient OG obtained 1 h (A) and 29 h (B) following injection into the skin of the midportion of the left back. There is transient uptake in the lymph nodes of the left axilla (A, arrow). This patient was proved to have no nodal metastases. Activity scattered from the injection site is evident in the lower margins of both panels. Note the greater background activity at 29 h, due to circulating antibody absorbed from the injection site.
Fig. 7. Posterior images of the thorax and upper lumbar area of Patient PH taken 20 min (A), 6.5 h (B), and 24 h (C) after injection into the skin of the midback. Axillary nodes were not palpable and were free of melanoma. There is early uptake into both axilla, right greater than left (arrows, A). The lymphatic drainage tracts can be seen faintly, extending to the axilla on either side of the injection site (short arrows). In B, the left axillary activity has disappeared at 6.5 h, and the right axillary activity has partially cleared (arrow). Splenic uptake has become evident (small arrow). At 24 h, there is only faint uptake in the right axilla (arrow). Injection site (l) is persistently visualized despite shielding due to the high energy of the $^{131}$I.

Fig. 8. Decay-corrected nodal time-activity curves where obtained. Note the considerable overlap between tumor-involved and tumor-negative nodes seen at early times but which does not persist, or the tumor-involved nodes continue to accrete and retain the antibody to a greater extent than the tumor-negative nodes, which lose the radioactivity over time. ROI, region of interest.

Involvement in palpable nodes in one of the clinical Stage II patients. Whole body images were obtained in all patients, but no nonnodal foci of uptake were seen to suggest metastases. Thyroidal, urinary tract, and occasionally some splenic and intestinal uptake of excreted $^{131}$I were seen, however.

Excised Nodal Radioactivity

The median percentage injected dose per node of the $^{131}$I 763/225 mixture from resected tumor-positive nodes was much (24-fold) higher than that in the tumor-negative nodes ($P < 0.001$) (Table 3). This was also true on a per g basis where the tumor-positive lymph nodes have a median 0.01984% injected dose/g and the tumor-negative nodes which have a median 0.003215% injected dose/g, based on our experiences with 533 lymph nodes ($P < 0.01$). From 8 patients 283 lymph nodes were removed in which the $^{125}$I nonspecific antibody was coadministered with the $^{131}$I specific antibody cocktail. These nodes show roughly 5-fold less uptake of nonspecific antibody than specific antibody and do not show a statistically significant difference between nodal uptake in the tumor-positive and tumor-negative lymph nodes on a per node or per g basis. There may be preferential uptake of the nonspecific antibody in the tumor-positive as compared to the tumor-negative nodes, compatible with our knowledge that tumor-positive nodes are larger than tumor-negative nodes, although the differences did not achieve statistical significance in this smaller number of nodes (Table 3).

Autoradiography

Contact autoradiographic studies showed at least two patterns of $^{131}$I uptake: obvious uptake in the tumor in the tumor-involved lymph nodes was seen in several instances (Fig. 9); but in other instances, nontumorous antibody uptake was seen in areas of nodal fibrosis or histiocytosis (Fig. 10).

Immunohistochemistry

All tumor-involved nodes stained ($N = 19$) with 763.24T and with 225.28S were antigen positive. The staining was more...
possible, in this small group of patients, to separate many of
the nodal tumor-positive from the nodal tumor-negative pa-

tients. Indeed, in two instances when the scan showed results
different from the clinical findings, the scan was in both in-
stances correct (once detecting melanoma in tumor involved
nodes, and once showing only minimal uptake of the antibody
in clinically palpable nodes subsequently shown to be pathol-

zymically negative). Since clinically palpable nodes in a nodal
group draining the primary lesion in a patient with melanoma gen-

erally represent melanoma (positive predictive value, 94%)

the probable clinical application of a fully optimized immunolym-

phoscintigraphic approach, would be in the population of clin-

cally Stage I patients, in whom the decision on whether to

perform surgery can be a difficult one, and in which a negative
clinical nodal exam may, in nearly 40% of cases, miss nodal

tumor involvement (28). Certainly, many more patients would

need to be studied to determine if the technique we have
described would be of clinical utility in selecting those patients
who may benefit from surgical resection, since the nonspecific

trapping of antibody in nodes not harboring tumor, as well as

nonaccessibility of tumor by antibody in some tumor involved

nodes remains problematic.

While limited in patient numbers, our results with immuno-

ymphoscintigraphy in melanoma are considerably more en-
couraging than those reported to date by other groups for this
disease (16–18), although they parallel preliminary successes in
lymphoscintigraphy with antibodies reported by others in breast
cancer and cutaneous T-cell lymphoma (13–15) and our expe-

rience in the nude mouse model of antibody lymphoscintigraphy
(29). We believe that the good results we report in these patients
are due to several factors including the choice of the low protein
dose antibody cocktail (which allows for additive binding to the
different high molecular weight antigen of melanoma epitopes
on the first pass through the lymph node), the choice of the 131
radioisotope (which does not appear to be actively sequestered
in lymph nodes as might be the case with radiometals), the use
of delayed imaging times to allow for nonspecific antibody

transiently sequestered in lymph nodes to clear (allowing for
the detection of the specific antibody signal), and due to our
p.l. antibody administration to more closely mimic the path of
lymphatic flow seen from the primary lesion (as opposed to
injection at some distance from the primary lesion, which
potentially may deliver antibody to nodes that may not accu-

rately represent those draining the primary). Still, the technique
is imperfect, inasmuch as nonspecific antibody binding in lymph

nodes remains somewhat problematic, although this may be
addressable in part by antibody fragmentation in which we have
seen lower nonspecific nodal uptake with Fab fragments, which
also deliver a lower injection site dose than intact antibody

(30). Of note is that our injection site clearance rate data

Discussion

This Phase I study of 17 patients with melanoma indicates
that the low protein dose, 131 anti-melanoma monoclonal an-
tibody cocktail can be administered safely and that it accumu-
lates in melanoma-involved lymph nodes roughly 24 times more
than it does in tumor-negative nodes. The tumor uptake of
specific antibody is also considerably greater than that of non-
specific antibody. Further, by external gamma scans, with par-

ticular attention qualitatively and quantitatively to the clearance
rate of antibody from the nodal groups, it appears commonly

intense when both antibodies were combined, as would be
expected due to their additive binding. No shed antigen was
detected immunohistochemically in multiple non-tumor-in-

volved nodes, even those with retention of radioantibody.

Fig. 9. Autoradiograph and histological section from a node not involved
with tumor. There is extensive histiocytosis apparently resulting in the retention
of radiolabeled antibodies.

Table 3 Uptake of radiolabeled antibodies by excised lymph nodes

<table>
<thead>
<tr>
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<th>Tumor-positive nodes (N = 21)</th>
<th>Tumor-negative nodes (N = 512)</th>
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<tr>
<td></td>
<td>Mean ± SEM</td>
<td>Median</td>
</tr>
<tr>
<td>Wt (g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>131 uptake % ID* /node (763-225)</td>
<td>0.03105 ± 0.00939</td>
<td>0.01217</td>
</tr>
<tr>
<td>131 uptake % ID/g (763-225)</td>
<td>0.04336 ± 0.02089</td>
<td>0.01984</td>
</tr>
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</table>

131 uptake % ID/node (sheep IgG) | 0.00749 ± 0.00358 | 0.00430 | 1.38 | NS        | 0.00022 ± 0.00003 | 0.00010  |
| 131 uptake % ID/g (sheep IgG) | 0.00962 ± 0.02089 | 0.00356 | 1.13 | NS        | 0.00184 ± 0.00017 | 0.00092  |

* % ID, percentage of injected dose; NS, not significant.
parallel those of our animal studies: the extremities are faster than the abdomen; but the mean clearance rate in humans is overall slower than that seen in animals (30). Similarly, while our absolute percentage of injected dose/g of specific antibody reaching the tumor of approximately 0.02%/g at 72 h is not as high as we would prefer, it is among the highest reported for murine antibodies given to humans, supporting the value of the regional antibody delivery approach versus systemic administration i.v., where not uncommonly 0.001% of the injected dose/g reaches tumors postinjection (31, 32).

In summary, the feasibility of specific detection of tumor-involved lymph nodes preoperatively in patients with melanoma through the use of a low dose antibody cocktail immunolymphoscintigraphic approach has been demonstrated in this study. While the technique is imperfect, the results are encouraging and, if confirmed in a larger study, this type of diagnostic approach may ultimately have clinical utility as a method for directing the management of the patients with Stage I melanoma. It is certainly possible that this low dose antibody cocktail lymphoscintigraphic approach, with the appropriate choice of antibodies, may be applicable to other illnesses in which the staging of nodal metastases is of clinical importance.

Acknowledgments

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References


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