An Algorithm to Adjust a Rigid CT-SPECT Fusion so as to Maximize Tumor Counts from CT VoI in I-131 Therapies

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Abstract-- The accuracy of the estimate of tumor I-131 activity in therapy patients using CT-SPECT fusion is difficult to establish. In our work, we have had the impression that a tumor volume of interest (VoI) from CT sometimes does not perfectly overlay the true position of the tumor in the SPECT image set. However, the magnitude of the difference between the activity estimate from the procedure and that from a perfect overlay is uncertain. Although we have not estimated that magnitude, we have investigated how much the activity estimate increases if we apply a last variation on the fusion to change the location of the tumor VOI so as to increase tumor counts. The results show that the algorithm can be effective in registering tumors in CT and SPECT locally as proved by visual checks of the optimized location of the tumor VOI in SPECT. For 14 tumors in seven patients the increases in tumor counts average 6.65%. The max increase is 26.7%.

I. Introduction

Accurate estimation of tumor activity is of great importance in therapy planning and response monitoring in nuclear medicine. Single-photon emission computed tomography (SPECT) is widely used as the functional image. To better quantify tumor activity, it may be helpful to integrate anatomical information (CT images) with the functional data. For example, Kramer et al [1] early on used CT-SPECT fusion to identify anatomic sites in the SPECT image set. This usage can be especially important with I-131 SPECT due to its usually low resolution.

Our activity quantification procedure for patients has been characterized in print [2,3]. First, filtered backprojection produced an initial SPECT reconstruction without attenuation correction. A patient CT image set was then fused with this SPECT image set. That is, CT values were transferred into the SPECT image space. (There they were converted to attenuation coefficients). Call the transformation involved T. Transformation T usually came from a fusion based on maximizing the mutual-information between the two image sets (6 of the 7 patients discussed here), or, in rare cases from a fusion based on least mean square error between pairs of internal markers. The "MIAMI fuse" software developed by Chuck Meyer was used to accomplish either type of fusion [4]. Warping was never utilized so the fusion was restricted to a rigid rotate-translate transformation. However, the radius for the multi-dimensional vector which defined the limits for a new set of control points for a new iteration, as well as the ultimate stopping criterion, was varied by the operator in a search of the "best overall" fusion.

For abdominal scans, 1) the locations of the liver and spleen, which both had considerable uptake, were taken into account in judging the fusion quality, and 2) the location of the kidneys, which usually had some reduced uptake, was taken into account as well. The approximate location of abdominal tumors was not considered very much at first. The thought was to not bias the result. But it was used more as the processing of patients continued and the difficulty of judging what constituted a good fusion became more apparent. For the pelvis, the scanning of which came after considerable experience with scanning the abdomen, usually only the location of the tumors could provide guidance as to the quality of the fusion.

Eventually, the inverse of the T transformation was used to bring a final SPECT reconstruction back into the CT space where the tumor volumes of interest (VoIs) were available. However, the ultimate accuracy of the estimate of tumor activity based on this procedure was difficult to establish. Inaccuracy can be caused by "fusion error" which in turn comes from several factors. Depending on the type of fusion, these factors include: 1) a non-rigid change in the body habitus between CT and SPECT, 2) a change in the tumor location relative to the large organs or relative to the skin markers, 3) poor choice of the control points that initialize a MI fusion, 4) non-optimum choice of other parameters in MI registration, 5) failure of maximum MI to yield a good registration even with the optimal choice of input parameters.

In this paper, we explore the possibility of optimizing the tumor location in SPECT by a local variation on the inverse of the T transformation, with the criterion of maximizing counts in the VoIs of known tumors. This criterion is proposed because we assume the soft tissues, organs or any other objects adjacent to the tumor have a lower activity concentration than that in the tumor (however, see the Results section). The tumor activity estimated from the new location of the tumor VOI in the SPECT image set is then compared to the activity found from the inverse of the T transformation. The latter has up to this time been accepted for producing the activity quantification of patient data.

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0-7803-7324-3/02/$17.00 © 2002 IEEE

II. METHODS

A. Initial CT-SPECT Fusion, Final SPECT Reconstruction, and New Fusion

Describe a rigid 3-D fusion by a constant transformation matrix T. If $\mathbf{x}_0$ and $\mathbf{x}_1$ are the coordinate vectors of the CT image before and after the registration, the transformation equation is: $\mathbf{x}_1 = T \cdot \mathbf{x}_0$. After the initial rigid fusion and calculation of the attenuation map, the next step was to input the attenuation map, the raw projection data corrected for deadtime, and projection images that estimated scatter into the space-alternating generalized expectation-maximization (SAGE) iterative algorithm [5]. This algorithm reconstructed the final SPECT image set while compensating for attenuation and scatter. Let I_{SPECT} represents the final reconstructed SPECT image. The last step in the old procedure involved using the inverse of the transformation T to transform this SPECT image set into the CT space. In the CT space, the tumor VoIs were known and were applied to obtain total counts within the tumors. The new step introduced in this research involves allowing a new fusion, different from the inverse of the transformation T. This new fusion is designed to optimize the location of tumor VoIs on I_{SPECT}.

B. Local Optimization by Maximizing Counts in Tumor VOI

First, we generate a 3D binary image I_{VOI}, which is an indicator function, i.e.

$$I_{VOI}(x,y,z) = \begin{cases} 0 & (x,y,z) \notin \text{VoIs} \\ 1 & (x,y,z) \in \text{VoIs} \end{cases}$$

The new iterative fusion is then carried out: the image I_{VOI} is registered with I_{SPECT} so that the net counts inside the VoIs for tumors are maximized. The objective function L can be written as:

$$L_{obj} = \sum_{(x,y,z)\in\Omega} I_{SPECT}(T(x,y,z)) \cdot I_{VOI}(x,y,z).$$

where Ω is the image domain of CT. We use the Nelder-Mead simplex algorithm [6] to find the transformation matrix which can maximize the above objective function, i.e. $\hat{T} = \underset{T}{\operatorname{argmax}}\, L_{obj}$.

There are six degrees of freedom in the matrix T. Three of them are rotation angles and the other three are translation variables. The initial guess for the new iterative fusion is always the inverse of the first fusion.

C. Patient Image Sets Involved

We have implemented the algorithm described above and tested it on three groups of patients with lymphoma [2]. These patients had known tumors that were located either in the abdomen or the pelvis or in both.

The patient with ID#7 had two abdominal tumors and two pelvic tumors that were captured in a single camera field of view. We investigate a number of fusion variations for him in order to obtain a satisfactory result. Included among the variations is maximizing the counts in the abdominal tumors separately from those in the pelvic tumors and vice versa, as well as maximizing the counts in single tumors.

The starting point for the new count-maximization fusions reported on here was usually the fusion result that was accepted for the patient in our previous processing of the data for a dosimetric study [new JNM article, submitted]. This fusion result came from a fusion based on maximizing the mutual-information between the two image sets (CT and SPECT), or, in rare cases (one of the seven patients), on a fusion based on internal markers. Warping was never utilized in the fusion. The scale in all cases was based on previous calibration of the image space for both modalities. The fusion thus was restricted to a rotate-translate fusion. However, the radius for the multi-dimensional vector which defined the limits for a new set of control points for a new iteration, as well as the ultimate stopping criterion, was varied by the operator in a search for the "best overall" fusion. For the abdomen, 1) the locations of the liver and spleen, which both had considerable uptake, were taken into account in judging the fusion quality, and 2) the location of the kidneys, which usually had some reduced uptake, was taken into account as well. The approximate location of abdominal tumors was not considered very much at first in order to not bias the result, but was used more as the processing of patients continued. For the pelvis, usually only the location of the tumors could provide guidance as to the quality of the fusion. Due to software limitations, the exact location of the tumor outlines could only be applied to a final result. The location then was used as a final check on the fusion quality. If results were felt to be not good, another cycle of seeking a new fusion was initiated. At most, two final results with tumor outlines placed on the images, were generated and chosen between.

III. RESULTS

Figure 1 top shows a transverse slice from the x-ray CT image set for the patient with ID#62. A contour which was manually drawn by a radiologist outlines the right pelvic tumor, called "rpel," in white. To the left of Figure 1 bottom, the contour is shown on the final reconstructed SPECT which has been registered with the CT image by the inverse of the initial mutual-information-based registration. The location of the contour shows a mismatch between the VoI and what would appear to be the tumor location (that is, the location having high activity shown in red). To the right of Figure 1 bottom, the tumor VOI has been locally optimized by means of an inverse fusion based on the net max-counts criterion. The new registration of the VoI appears to be better than the initial result. Notice that although the figure only shows the result for a single 2-D slice, the optimization is performed in 3-D. The new count total for the entire tumor (including multiple 2-D slices) is shown in Table 1. The activity estimate for this tumor is proportional to this count total. The table also gives the tumor volume, the count total from the original fusion based on the inverse of the transformation T, and the percent difference. The table shows that for patient 62 there is a substantial increase for two of her three tumors. For the

other patient, there is only a moderate increase in his one tumor.

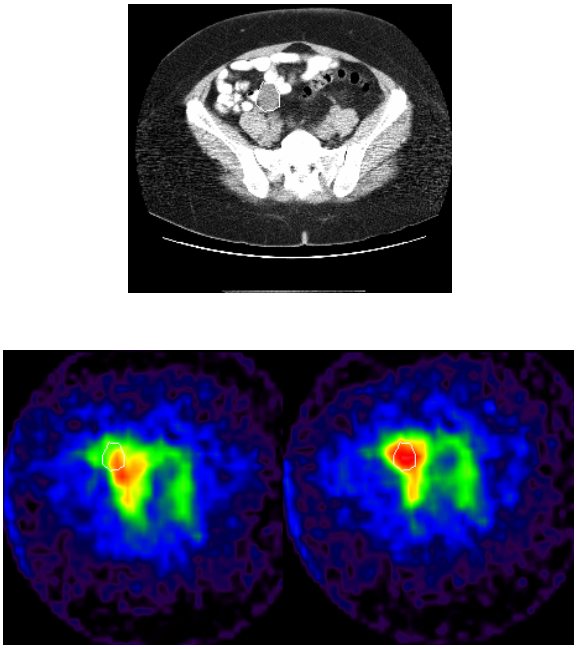

Figure 1. CT image (top) and old and new fusion result (bottom) for patient 62.

Table 1. Results from net-counts maximization for patients with pelvic tumors.

Patient ID#	Tumors	Volume cm^3	Original Counts $\times 10^{12}$	New Counts $\times 10^{12}$	Change %
62	"rpel"	330	1.07	1.28	+19.6
	"lpel"	316	1.11	1.15	+3.87
53	"big"	281	1.38	1.43	+3.62

The results from the patients with abdominal scans are given in Table 2. The net count for their tumors is maximized in each case. For two patients, the percent increases are small. For one patient, the percent increases for his two tumors are more substantial (18 and 7.5%). For the last patient, the increase in his large tumor is moderate (3%), but there is actually a large decrease in his small tumor (30%). Visually, the new result for the patient with ID#66 appears to be an improvement, although the images aren't shown.

Figure 2 shows one 2-D slice from the fusion that maximizes the net count for the two abdominal and the two pelvic tumors in the patient with ID#7. One sees that the "big" tumor and the "lf" tumor, the two abdominal tumors, both seem correctly positioned next to the aorta which separates them and which probably has considerable activity remaining in the blood it contains. The kidney VoIs appear

Table 2. Results from net-counts maximization for patients with abdominal tumors.

Patient ID#	Tumors	Volume cm^3	Original Counts $\times 10^{12}$	New Counts $\times 10^{12}$	Change %
2	"inf"	68.9	0.210	0.248	+18.1
	"sup"	33.8	0.160	0.172	+7.50
14	"kid"	53.6	0.804	0.804	+0.00
	"ant"	40.2	0.546	0.547	+0.183
47	"laor"	13.2	0.0439	0.0440	+0.228
66	"big"	299	3.00	3.09	+3.00
	"post"	17.2	0.128	0.0902	-30.0

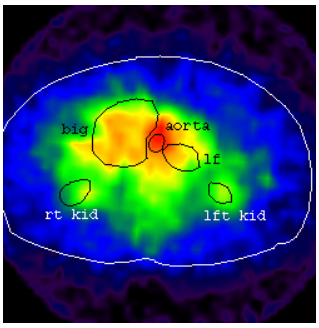

Figure 2. The net-count-maximization result for the patient with ID#7. SPECT slice corresponds to CT IM 41.

positioned in approximately the correct place, although they give the impression that the horizontal scale, which is set by a camera calibration and not adjusted by the fusion, may have changed from when it was measured and is slightly incorrect. The tumors do not appear to have a completely uniform activity distribution (some regions are red or orange, but others are green denoting lesser activity), but that is not surprising. The count totals for all 4 tumors from this fusion are shown in Table 3. The count changes for the abdominal tumors are encouraging. For "big," the increase in counts is 25.2% and for "lf" it is 8.94%.

Table 3. Results for a patient (ID#7) with tumors in both the abdomen and pelvis from net-count maximization of all 4 of his tumors.

Tumors	Volume cm^3	Original Counts $\times 10^{12}$	New Counts $\times 10^{12}$	Change %
"big"	455	2.19	2.74	+25.1
"lf"	135	0.770	0.839	+8.96
"lfplv"	111	0.449	0.663	+47.7
"rtplv"	6.8	0.0419	0.0327	-22.0

However, the count changes for the pelvic tumors are not as encouraging as those for the abdominal tumors. That is, the "lfpel" tumor count goes up by 47.3% but the "rtpel" tumor count goes down by 22.1%. Since the pelvic tumors have less counts by about an order of magnitude than the abdominal tumors, it is likely their count is not influencing the fusion very much and so their result is less reliable.

Also, due to the good possibility of a body flexion at the boundary between the abdomen and pelvis that was different for the SPECT scan compared to the CT scan, it makes sense to consider the results of a fusion that maximizes the counts in the lower part of the abdomen independently of those in the upper part of the pelvis, and vice versa. Such count-maximization fusions were carried out for this patient.

Table 4. Results for counts in abdominal tumors for patient ID#7 using different tumors, or different tumor combinations, for the count maximization.

Tumors used in maximizing counts	"big"	"lf"
	% change	% change
"big"	+31.7	-11.6
"lf"	-5.08	+14.9
"big" and "lf"	+23.5	+4.79
all 4 tumors	+25.2	+8.94

When a maximization of only the counts for the two abdominal tumors is performed, a slightly different fusion is obtained, but the count increases are almost as great as with the fusion based on maximizing the counts in all 4 tumors (23.5 compared to 25.2 for "big" and 4.79 compared to 8.94 for "lf" as shown in Table 4). Therefore, either new fusion probably produces activities that are closer to the true value and should be accepted. For our summation statistics given in a paragraph below, we use the higher values.

Table 5. Results for counts in pelvic tumors for patient ID#7 using different tumor combinations for the count maximization.

Tumors used in maximizing counts	"rtpel"	"lfpel"
	% change	% change
"rtpel" and "lfpel"	+6.24	+26.7
all 4 tumors	-22.1	+47.3

A separate fusion for the pelvis appears to provide a better result than the 4-tumor-count-maximization fusion as well. The count results for the pelvic tumors with this technique are shown in Table 5. This time, there is an increase for both pelvic tumors.

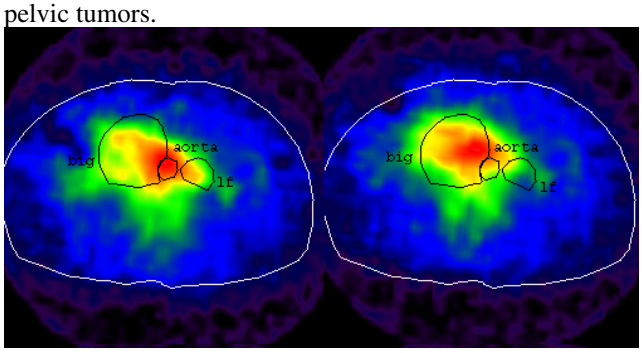

Figure 3. The net-count-maximization result for the patient with ID#7. SPECT slice corresponds to CT IM 43. left) Result for fusion that maximized counts in 2 abdominal tumors. right) Result for fusion that maximized counts in "big" which is unacceptable.

Figure 3 and Table 4 show the danger of accepting a fusion that maximizes the counts in a single tumor. The patient is the same as in Figure 2, but the SPECT slice is that 2cm more towards the feet. Figure 3a shows the result from the fusion that maximized the counts in the two abdominal tumors that was discussed above. Figure 3b shows the result from a fusion that maximized the counts in an individual tumor, namely "big." In the left of Figure 3, the outlines for "big," "lf" and "aorta" appear reasonable. In the right of Figure 3, the SPECT image seems to be shifted up and to the left. The VoI for "big" gets more counts incorrectly by being placed partly over the aorta. So, the potential increase in counts of 31.7% listed in Table 4 probably represents an increase that isn't consistent with reality and so is a result that shouldn't be accepted. The fact that the counts in the nearby tumor go down is added proof. Such a mixed result also occurred when the counts in the "lf" tumor was used as the basis of the maximization. So, such a procedure should be used with care even when the search range from iteration to iteration is fairly small, since there are erroneous ways in which the count estimate for a single tumor can be increased when its max counts is the sole criterion for the fusion. In particular, the results from the procedure are not preferred for this patient.

When the "best" values as described above are used for all 14 tumors in all seven patients, the positive % change ranges from 0.0 to 26.7. There is one negative % change equal to –30%. The average value over the 13 tumors with positive changes is 9.47% and over all 14 tumors is 6.65%.

IV. Discussion

We have chosen to maximize net counts in one or more tumors to carry out the inverse transformation (from SPECT space into CT space) in the tests above. Another possibility would be to maximize net counts in one or more tumors combined with one or more organs, such as the liver and kidney. Alternatively, one could choose to maximize the net percent increase in counts in the tumors involved. When there are at least two tumors with different count levels, this procedure would tend to prevent the high uptake tumor from dominating the registration. Another approach would be to use mutual information as the criterion for the inverse transformation instead of the criteria we have investigated. If the tumor VoIs were present in the color-wash display (which is basically possible) it would be easier to choose a good inverse fusion. Still another approach would be to combine the max-counts criterion with the max-mutual-information criterion to produce a joint objective function. With such a joint objective function, a weighting factor relating the two parts of the objective function would have to be chosen. This variation might be more stable, but it is less straightforward because it isn't clear what weight might be appropriate.

The count-maximization approach has a problem when a single tumor lies immediately next to a highly active object, like the bladder. However, the algorithm can be used in the pelvis when there are tumors on opposite sides of the bladder. Then, for example, a simple translation to the left increases counts in the tumor to the right of the bladder, but at the same time decreases counts in the tumor to the left of the bladder, precluding such a translation.

V. ACKNOWLEDGMENT

This work was supported by Grant R01 CA87955 awarded by the National Cancer Institute, United States Department of Health and Human Services. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Cancer Institute.

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