Automated Lesion Detection and Quantitative Response Assessment of Diagnostic CT Images

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Introduction

Previous AIQ-sponsored white papers have revealed how metastatic lesions can be detected and tracked to measure response using positron emission tomography (PET)[1-3]; however, only a minority of patients receive PET scans consistently throughout treatment. Most patients receive computed tomography (CT) scans alone to diagnose disease and assess treatment response, so the translation of AIQ's technology to CT is significant.

Until now, the use of CT in clinical trials has been guided by the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines which focused on target lesions, and limited evaluations to the measurement of the long and short axis diameter in a maximum of five lesions[4-5]. There are many problems with the RECIST criteria, first is the inconsistency of target lesion identification. To properly identify the largest lesions on a scan, all lesions should be measured, which is not feasible in highly metastatic patients. This causes there to be variations in which target lesions are chosen[6-7]. Additionally, the limited evaluation of only five lesions can miss underlying intra-patient (within subject) heterogeneity of treatment response that could be detected by evaluating all lesions. The identification and measurement of all lesions is time consuming and therefore clinically infeasible without automation. Furthermore, imaging metrics such as volume or texture analysis have been shown to outperform RECIST guidelines for survival prediction[8,9]. An automated solution for analysis of CT images is required to fully understand how patients are responding to treatment. AIQ's software technology fills this need as it automatically detects and quantifies lesions using diagnostic CT images, and measures lesion-wise response over multiple scans.

Lesion Detection and Concordance

In patients with a variety of metastatic cancers, AIQ's technology automatically detects lesions in bone, lymph node, liver, breast, lung, pancreas, bowel, and kidney using diagnostic CT images. AIQ has developed a set of deep learning lesion detection models specific for diagnostic CTs. Detection of colon, liver, pancreas, kidney, and lung lesions was assessed in cohorts of 26, 27, 60, 57, and 187 patients, respectively. The median patient sensitivity and number of false positives can be found in Table 1. Colon lesion detection was assessed in 26 patients with a median of 1 lesions per patient (range 1-2) on contrast-enhanced CT images. Detection sensitivity ranged from 0-100% with a median of 100%. Liver lesion detection was assessed in 27 patients with a median of 5 lesions per patient (range 0-42) on contrast-enhanced CT images. Detection sensitivity ranged from 50-100% with a median of 91%. Pancreas lesion detection was assessed in 57 patients with a median of 1 pancreatic lesion per patient (range 1-1) on contrast-enhanced CT images. All lesions (100% sensitivity) were detected in 49/57 patients. Kidney lesion detection was assessed in 60 patients with a median of 1 kidney lesion per patient (range 0-3) on contrast-enhanced CT images. All lesions (100% sensitivity) were detected in 57/60 patients; two of the remaining patients had no lesion detected (0/1 lesions; 0% sensitivity) and one patient had one lesion detected (1/2, 50% sensitivity). Lung lesion detection was assessed in 187 patients with a median of 3 lung lesions per patient (range 0-32) on non-contrast-enhanced CT images. 115 of the 187 patients had all lung lesions detected (100% sensitivity) and 20 had >50% sensitivity. Nine patients had no lung lesions

detected when there was 1-6 lesions present (1 lesion: N=4, 2 lesions: N=4, 6 lesions: N=1). All organs had high median detection sensitivity (≥90%) and low false positives/patient (0-3).

Table 1 Lesion detection sensitivity and average false positives (FP, identifications) per patient.

Organ	Sensitivity Median [IQR]	FP/image Median [IQR]
Colon	1.00 [1.00, 1.00]	1.5 [1, 3]
Liver	0.91 [0.50, 1.00]	0 [0, 3]
Kidneys	1.00 [0.00, 1.00]	0 [0, 2]
Pancreas	1.00 [1.00, 1.00]	0 [0, 0]
Lung	1.00 [0.67, 1.00]	1 [0, 3]

The concordance of lesion detection between PET and CT images was evaluated in 13 patients with metastatic breast cancer. Example concordance maps of lesion detection by PET only, both PET and CT, and CT only are shown in Figure 1. A population view of this concordance can be seen in Figure 2. With the exception of three patients, the majority of patients' disease (>70%) was detectable on diagnostic CT imaging.

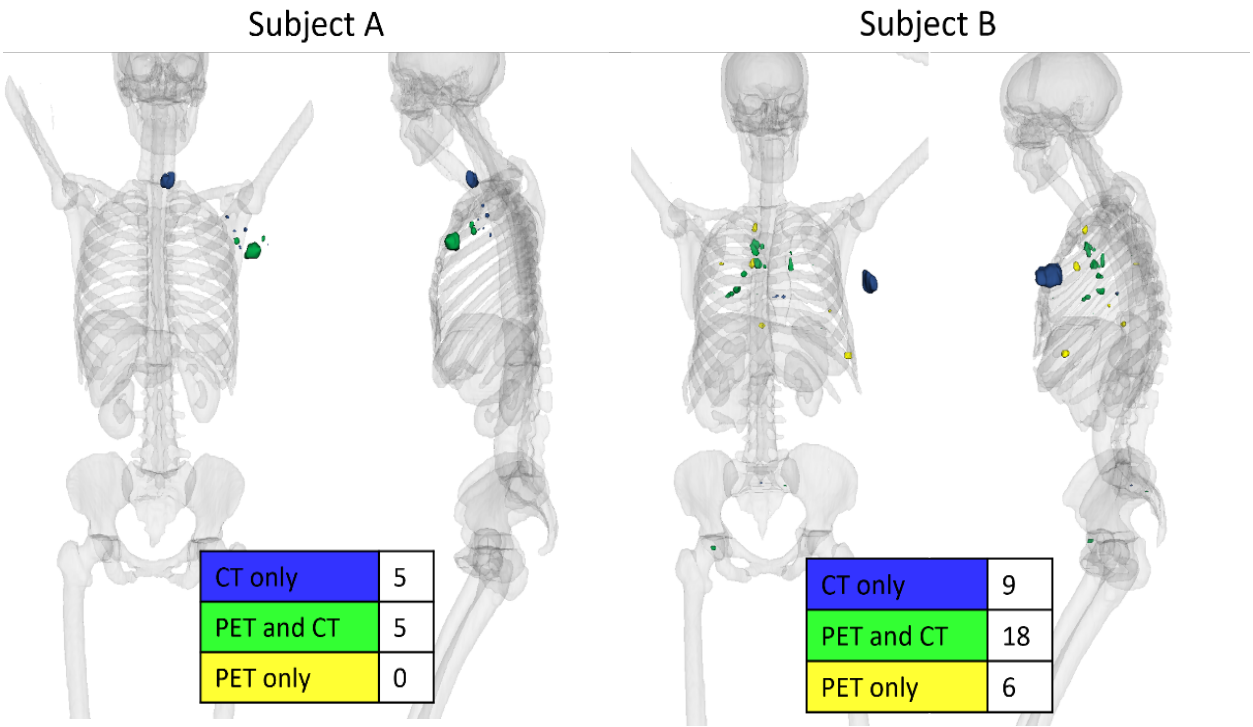


Figure 1. Lesion detection by modality (lesions detected on PET only, both PET and CT, and CT only) in two patients with metastatic breast cancer. Lesions are in bone, breast, and lymph nodes.

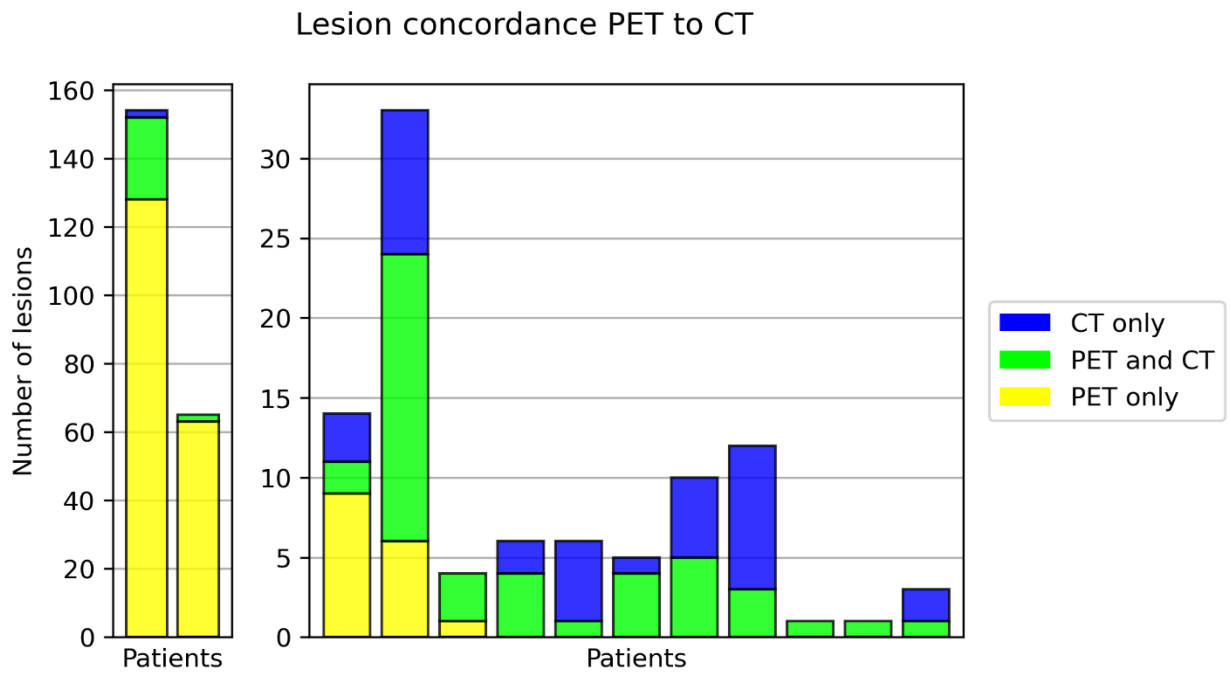
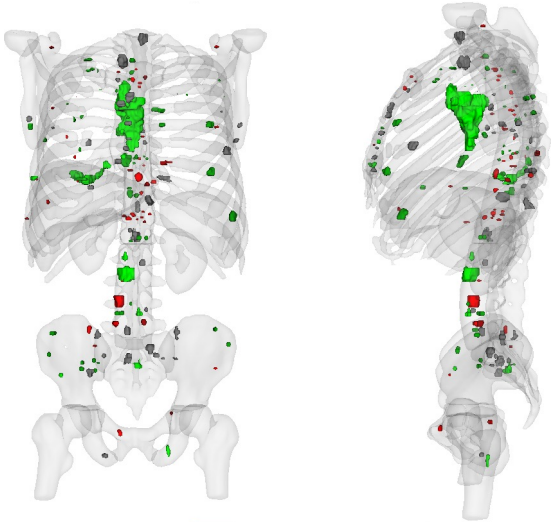


Figure 2 Concordance between detection of lesions using PET only, CT and PET, and CT only for all patients with metastatic breast cancer.

Treatment Response Assessment

In a study of 10 metastatic cancer patients, lesions were classified as disappearing, decreasing in volume, stable, increasing in volume, or newly appearing. Figure 3 shows an example of lesion response classification according to the change in volume as detected and measured on diagnostic CT images. All patients had some non-favorably responding lesions (increasing in volume and/or new disease) while 9/10 also had favorably responding lesions (disappearing and/or decreasing in volume) as shown in Figure 4. Response heterogeneity, defined here as the presence of both shrinking (responding) and growing/new (non-responding or progressing) lesions in a patient, was observed in 9/10 patients in this population. These lesion-wise response maps can be used to determine when to change systemic therapies and/or when to supplement a systemic therapy with a targeted local therapy (i.e., to control a small number of non-responding lesions). Response to treatment can be quantified according to many different metrics including short axis diameter (RECIST), long axis diameter, lesion volume, or average or maximum Hounsfield Unit (HU) density.



Response	Number of Lesions
New	21
Δ Volume > 30%	28
-30% ≤ Δ Volume ≤ 30%	39
Δ Volume <-30%	11
Disappeared	59

Figure 3 Example response map based on the change in volume of individual lesions in a patient with metastatic neuroendocrine lung cancer.

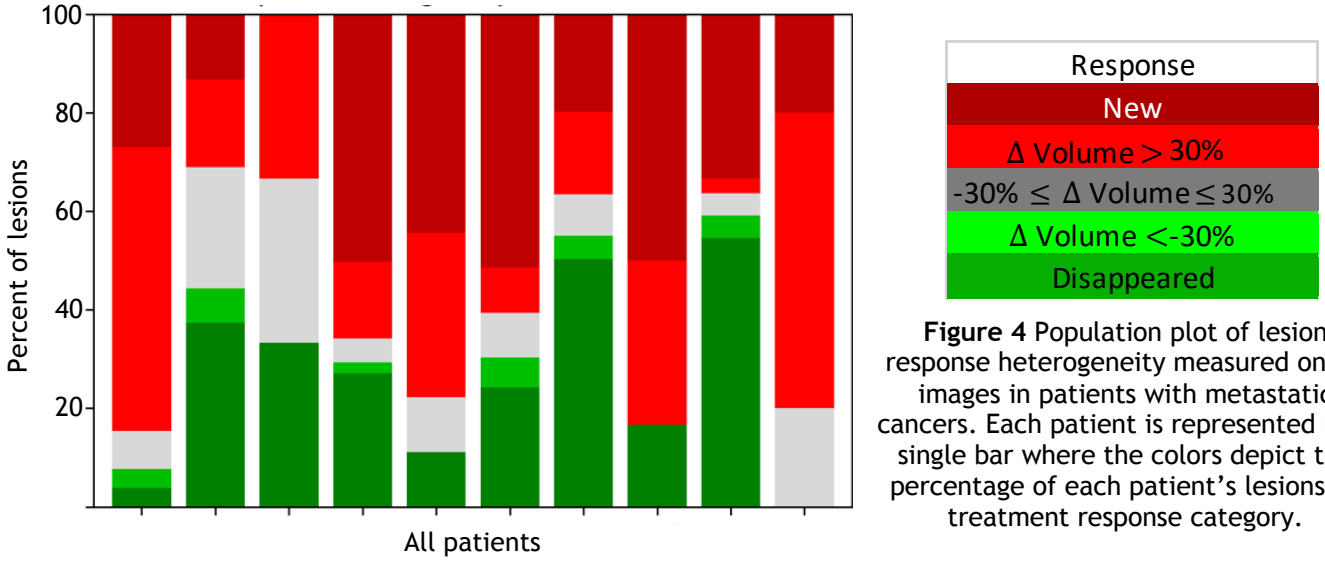


Figure 4 Population plot of lesion response heterogeneity measured on CT images in patients with metastatic cancers. Each patient is represented by a single bar where the colors depict the percentage of each patient's lesions by treatment response category.

Conclusions

Intra-patient heterogeneity of treatment is increasingly recognized and new treatment options targeting the emergence of early treatment resistance are being developed[10]. The studies outlined in this paper demonstrate the ability of AIQ technology to detect and segment lesions, quantify lesion-wise response, and assess treatment response heterogeneity on diagnostic CT images with or without contrast-enhancement. The AIQ technology was tested in lesions located in the bone, lymph node, liver, breast, lung, and kidney. This technology enables the medical community to quantitatively evaluate all of a patient's disease throughout care using standard of care diagnostic CT images.

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