



Cancer Monitoring: Find – Fight – Follow

Imaging is becoming a popular instrument across all areas of disease management – from initial diagnostic findings to therapy control. Take cancer, for example: After diagnosis, images acquired later show whether the tumor was treated successfully or has recurred. This information, supported by new software tools, determines subsequent procedures.

By David Tenenbaum and Hildegard Kaulen, PhD



With the new software, automated comparison of tumor burden, growth or shrinkage becomes more precise.

With *syngo*® CT Oncology and *syngo* TrueD, Siemens Medical Solutions developed two valuable software packages for monitoring cancer. *syngo* CT Oncology includes set algorithms for the segmentation of lesions in the liver, lungs, lymph nodes, and other regions of the body in computed tomography (CT) images. The software calculates various tumor parameters and compares them with subsequent diagnostic findings. As a result, tumor burden, growth parameters, and

other values can be tracked. *syngo* TrueD was developed for hybrid imaging using positron emission tomography-computed tomography (PET-CT) or single photon emission computed tomography-computed tomography (SPECT-CT). As a result, data sets from PET-CT examinations acquired at two or three time points are automatically registered for an on-screen comparison. Leading cancer centers are working with these two software tools.

Summary

Challenge:

- Increasing amount of data produced by medical imaging
- Difficulty to compare primary and follow-up studies for judging treatment response in oncology
- Different criteria for measuring treatment response (RECIST, WHO)
- Measuring and comparing studies are time-consuming processes

Solution:

- Automated follow-up with *syngo* TrueD (for PET-CT) and *syngo* CT Oncology (for CT)

Result:

- Software enables comparison of changes in metabolic activity as well as tumor burden, growth or shrinkage
- Studies are planned to evaluate tumor volume as criterion for treatment response



“The new *syngo* CT Oncology software is a much faster way of comparing and analyzing data.”

Vahid Yaghmai, MD,
Associate Professor of Radiology,
Northwestern University,
Feinberg School of Medicine,
Chicago, IL, USA



Let the Computer Do It: Fully Automated Tumor Tracking

Before data becomes information, it must be thoroughly examined and analyzed. As computed tomography (CT) scanners produce a growing torrent of data, radiologists confront a data-or-information question every day: how to obtain the maximum patient benefit from the hundreds of slices that an advanced CT scanner produces from each patient scan? Rigorous, accurate, and repeatable analysis of CT scans is a matter of life and death in oncology, but the sheer quantity of data raises the potential for operator fatigue and even error, and it also raises workflow headaches at the management level. All of these hazards are multiplied by the regular follow-up studies needed to track

tumor response to treatment. But wading through data is precisely why computers were invented. Several years ago, Siemens CT applications gained the capability to automatically detect tumors. Now, the new *syngo*® CT Oncology software has the capability to automate lesion measurement, routinely calculate tumor volume, and support a wide range of the data-handling operations necessary for top-flight medical care.

Quick, Accurate, and Consistent

In preliminary tests, Vahid Yaghmai, MD, Associate Professor of Radiology at the Northwestern University Feinberg School

of Medicine in Chicago, IL, USA, says this new software matches the best human measurements: “In our experience, we have seen an excellent correspondence between a manual measurement of lymph node tumors and most liver tumors, and the automatic software measurement. It’s very quick, accurate and consistent in measuring lesions using the RECIST [Response Evaluation Criteria in Solid Tumors] and WHO [World Health Organization] standards.” Yaghmai is also Medical Director of CT at Northwestern Memorial Hospital – Northwestern University, a tertiary care hospital in Chicago with one of the largest oncology units in the United States. In May 2007, he reported to the American Roentgen Ray Society that manual and automatic segmentation and measurement of abdominal and pelvic lymph nodes corresponded closely, according to both RECIST and WHO criteria. Similarly, he reported to the Society of Gastrointes-



tinal Radiologists that the software successfully segmented and measured 22 liver lesions on contrast-enhanced CT scans from 12 patients.

Simplified Follow-ups

Another key advantage of *syngo* CT Oncology is evident in its many improvements in throughput and workflow. To obtain automated measurements from *syngo* CT Oncology, a radiologist clicks on the lesion on the display and immediately receives a readout of x, y, and z dimensions, RECIST and WHO measurements, and lesion volume. Flexibility is the key to *syngo* CT Oncology software, and Yaghmai stresses that it does not take decisions out of the doctor's hands, but rather allows the physician to use preferred measurement standards. "The software can segment out the tumor and correctly measure it, providing RECIST, WHO and volumetric data

– so the doctor can use whichever he or she wants."

A further advantage is ease of follow-up. "The software is capable of comparing previous measurements with new measurements," says Yaghmai. "It's a much faster way of comparing and analyzing data." On follow-up scans, the system displays previous data on the same lesion, and calculates any dimensional change during the interim. "In a large oncology center, measuring lymph nodes in multiple dimensions and reporting on multiple lesions in every study is a very time-consuming process," says Yaghmai. "An automated way of measuring lesions would really improve workflow. You decide which lesions to evaluate, and click on as many as you want. Theoretically, somebody who is not a radiologist can look at those lesions on a follow-up study." This simplified follow-up is one of the most significant benefits of this new *syngo* software;

there is no need to 'find' the same tumor on previous images and then determine which slice shows the greatest single dimension for RECIST or WHO measurements – those repetitive functions are now all embedded in the software. "When you follow patients based on these measurements, you want consistent and reliable data, and this software provides it. It virtually eliminates human error and the variations in measurement that can occur when doing it manually," says Yaghmai. "Despite advances in technology, consistency remains a problem in radiology. There have been many studies showing that measurements of the same lesion by two observers will be different. *syngo* CT Oncology eliminates that part of the inconsistency." This improvement may be particularly important in irregular tumors with poorly defined margins that are difficult to measure.

Better Patient Care

On the practical level, automated measurement can also improve the accuracy of comparisons when patients change hospitals. "Many patients are first imaged at a small community hospital," says Yaghmai. "The National Cancer Institute is pushing for us to standardize the way we follow up tumors. There really is a lot of variability in how different centers do follow-ups, and we want to standardize how we acquire images and measure these tumors. Automated measurement can also advance the state of the art in oncology by improving the accuracy of tumor assessment during clinical trials." Greater accuracy may also help resolve long-standing questions about the relative value of RECIST and WHO standards. Most of the debate stems from the issue of human error in manual segmentations. *syngo* CT Oncology also addresses a key issue in radiology: fatigue. "Operator fatigue is always a huge issue in radiology," says Yaghmai, "especially with the increasing number of slices – from several hundred to a thousand per study. Fatigue has a lot to do with it. And there, the num-

ber of CT scans obtained in large centers like ours is increasing.”

Volume as a Standard Modality?

Fast, accurate, and repeatable tumor segmentation and measurement are significant advances, but *syngo*'s new ability to automatically calculate tumor volume could have equal importance. Studies have already shown that the volume of lung tumors may be valuable for assessing progression or regression; similar studies for liver, bone and brain tumors remain to be completed. Although the role of volume in determining tumor status remains subject to further research, “Intuitively, we think it should be important,” says Yaghmai. “But until now, the difficulty of performing volume measurements has limited our ability to validate this.”

In the longer term, automated tumor measurement can take radiology firmly into the third dimension. While each component of a CT scan is a two-dimensional slice of the patient's anatomy, tumors themselves are three-dimensional objects, and the newfound ability to automatically measure volume will allow comparisons to see whether volume, RECIST or WHO is most appropriate for evaluating treatment. Volume is a particularly difficult issue in

small lesions, which are difficult to measure manually, and where a slight error in measurement can lead to a significant error in volume calculations. “When you measure a small tumor manually, because it is less spherical and has more irregular margins, the measurement will be more prone to error,” says Yaghmai. “Since the software can segment out lesions that are quite small, you eliminate that variability,” he explains, adding that furthermore, some studies indicate that as a tumor gets smaller, volume should play a more important role in follow-up. Here, too, automated measurement may provide an improvement in accuracy.

Although the exact implications of volume measurements in terms of patient management for tumors of the liver or lymph nodes remains to be seen, Yaghmai stresses that accuracy and repeatability have immense value in improving patient care. “We do not want the human factor to be a component of these measurements,” he says. “It's better for the patient to have realistic information. Whether or not volume becomes a standard modality for evaluating treatment, software like this will eventually be standard for any follow-up of oncology patients. Previously, the technology was not available, but now it is.”

Master of Comparison in Hybrid Imaging

In PET-CT (positron emission tomography-computed tomography), metabolic images are superimposed on anatomical images. Using this hybrid-imaging method, tumors are no longer detected merely by appearance, but through their metabolism as well. Using the *syngo*® TrueD software package, hybrid images acquired over a period of time can be compared and quantified on a display for the first time.

Medical Solutions spoke with Professor Bernd Joachim Krause, MD, of the University Hospital Rechts der Isar in Munich, and Andreas Wahl, MD, of the PET-CT Center in Hamburg, Germany, regarding its clinical potential.

Dr. Wahl, you are a nuclear physician and radiologist in private practice.

In your opinion, what is unique about *syngo* TrueD?

WAHL: The uniqueness of *syngo* TrueD is its ability to work with the large volumes of data associated with hybrid imaging while simultaneously providing a comparison mode. This integrated combination was not previously available. Either one or the other was possible. Using *syngo* TrueD, six data sets can be loaded – three CT scans and three PET examinations. We are now able to establish a direct relationship between images acquired at different points in time even from a quantitative

view. The software package provides a range of flexible screen layouts and tools. Automatic registration takes less than half a minute. This improves our workflow by reducing the time for handling and evaluating image data, helping the physician to focus on the relevant findings.

How do patients benefit from the comparison mode?

WAHL: Both accuracy and reproducibility in diagnosis as well as measurement comparisons are improved with using a software with specialized tools like *syngo* TrueD. And this is possible irrespective of whether standardized criteria such as

Left: Professor Bernd Joachim Krause, MD
Right: Andreas Wahl, MD





metabolic activity – calculated as Standardized Uptake Value (SUV) – longimetry according to WHO [World Health Organization]/RECIST [Response Evaluation Criteria in Solid Tumors] standards or measurements are being applied. The patient benefits from a precise calculation of response after chemo- or radiotherapy, for example, by means of elimination of technical errors that could otherwise cause an inadequate treatment. Additionally, the software package supports fusion with other images. This includes magnetic resonance, CT, PET, or SPECT [single photon emission computed tomography] images acquired at other facilities. This is

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PET-CT-Center, Hamburg, Germany

also of significant benefit, because comparison of the present PET-CT with these former (external) examinations is necessary for a correct diagnosis.

Professor Krause, you work at the University Hospital and also keep an eye on clinical studies. Where do you see the benefits of syngo TrueD?

KRAUSE: In recent years, we have seen that cancer is a heterogeneous disease. Individualized therapies are a main goal in the future. You may ask what that has to do with syngo TrueD. Allow me to explain. To develop individualized therapies, we need comprehensive information regarding their effect. Morphology alone is no longer sufficient. This is the reason why PET-CT is so important in oncology, because we learn something about both function and structure. For therapy control, we therefore have a great need for new criteria that allow assessment of therapy response – so-called surrogate parameters. To date, the primary orientation has been toward the diameter of the tumor lesion. But metabolic activity may be a much better surrogate parameter, especially if correlated with volumetric information, and if a fast comparison of two examinations over time is available for hybrid imaging. We gain sophisticated information and a completely different method of access to the timeline of a treatment. The task before us is very clear: We have to find reliable thresholds for

the segmentation of tumor lesions and changes of metabolic activity. That is, we have to see which grayscale values securely delineate the boundaries of a tumor or which percentage change in glucose metabolism indicates therapy response, and then create clinical studies that establish volume and metabolic values as surrogate parameters.

How has the response to radiation and chemotherapy been determined to date? Is diameter the only recognized surrogate parameter?

WAHL: WHO and RECIST criteria are established and can be used predominantly for solid, well-definable lesions with a minimum size. Those criteria are based on two-dimensional [WHO] or one-dimensional [RECIST] measurements in axial CT images. But applying those criteria to lesions that are hardly definable or very small is problematic and can easily involve relevant measuring inaccuracies. For tumors like GIST [gastrointestinal stromal tumor], which can increase in size during therapy, they cannot reliably evaluate

therapy response. In principle, a calculation of tumor volume by means of multislice spiral CT and the respective software algorithm is possible in much more detail. Functional information, for example from PET studies, is not considered in these criteria, although for some diseases [M. Hodgkin's, DLBCL-NHL], evaluation of therapy response would be helpful to them.

KRAUSE: The RECIST and WHO criteria have clear limits, as have been shown time and again. In addition, they are from a time when slice imaging procedures were not at the standard we have today. And we have gone a step further with hybrid imaging. What we lack now are clinical studies that show the value for the clinical routine of metabolism, volume or another surrogate parameter. Here, one can see clearly how development proceeds. First, the technical prerequisites are established. Then, clinical potential is investigated. I am absolutely convinced we will have different surrogate parameters for various tumor entities in the future. Volume will



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merely be one of many. In addition to maximum length and volume, other conceivable parameters include density, metabolism, and surface characteristics of a lesion for example.

Professor Krause, have you already planned concrete studies to show whether, besides metabolism, the volume of a tumor is a good surrogate parameter for therapy response as well?

KRAUSE: Yes, we have created a study to examine whether, using a combination of thresholds for metabolism with volumetric variables (among others, segmentation-based volumetry), achieves an even better prediction of tumor response to a therapy. We hope to see how close we come to reality with the software. I am excited!

In Germany, PET and PET-CT fall under private physician or individualized healthcare services, the only exceptions being staging, restaging, and follow-up for non-small cell lung cancer.

Their in-patient use is still difficult due to financial restrictions. What do you think about this situation?

WAHL: Approval of FDG-[¹⁸F-fluorodeoxyglucose-]PET for non-small cell lung cancer shows that its significance for oncology can no longer be negated. But presently, long consulting processes for this indication make prognoses for the approval of further indications difficult. However, with new modes of care in public health insurance, PET diagnostics may be established at least on a regional level.

KRAUSE: In Germany, we are dealing very cautiously with the potential of hybrid imaging because it does not have its own distinct billing codes, whereas in most other European countries, there is a general cost reimbursement. Fortunately, a change has been made in cost reimbursement for non-small cell lung cancer. However, we have another problem in Germany, that of positron emitters. Only ¹⁸F-fluoro-desoxyglucose – marked glucose – is approved. The use of other markers is difficult due to the German

Pharmaceutical Act. Positron emitters have to be approved as pharmaceuticals. I expect there will be a simplified approval process soon. Given the potential of hybrid imaging and the new capabilities provided by software packages such as syngo TrueD, that would be very desirable.

David Tenenbaum is a freelance science, medical, and technology journalist based in Madison, WI, USA. He is also the head writer for The Why Files, an electronic magazine covering “the science behind the news,” which was started in 1996 by the National Science Foundation and the University of Wisconsin.

Hildegard Kaulen, PhD, is a molecular biologist. After positions at Rockefeller University in New York and Harvard Medical School in Boston, MA, USA, she has worked since the mid 1990s as a freelance science journalist for well-known newspapers and scientific journals.

Further Information

www.siemens.com/ct-oncology
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