

Volumetric analysis more precisely checks cancer therapy response

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Methods to evaluate cancer progression – based on measurements of 2-D images of tumors – are key to determining if cancer therapies are working. Physicians have relied on this strategy for years. But a better, more accurate way is now available which quantifies the entire volume of tumors and lymph nodes.

Definiens (Munich, Germany and Parsippany, New Jersey) has just launched LymphExpert Version 2.0 in the European market, following CE-mark approval. LymphExpert is a software application that assists radiology professionals in the identification, analysis and evaluation of lymph nodes in CT images over time making use of volumetric analysis software, further automating the cancer diagnostic process.

“From a math perspective, there’s no disagreement with volume being more sensitive in assessing the change of an object compared with measurement of tumor diameter,” Frank Klein, VP of Medical Imaging at Definiens, told *Medical Device Daily*. “Even if you have a simple measure of diameter, it doesn’t tell you if the whole object has grown, but therapy continuation is based on that measure. With disease remission, there’s a decrease in size and volume. More than 50% of doctors would just visually inspect for growth or remission. We are trying to change that.”

And that change comes via a complex software analysis system.

Last summer Definiens launched a multidimensional image analysis platform called Definiens XD, capable of extracting previously unattainable levels of intelligence from digitized medical data. The launch of the XD platform marked a milestone in entering the medical imaging market (*MDD*, June 30, 2009).

The newest launch, LymphExpert, focuses on the lymphatic system, which analyzes lymph nodes in 3-D and visualizes their volume, providing a more complete picture when compared to current standards known as RECIST (response evaluation criteria in solid tumors) – which evaluates patient responses to treatment based on tumor diameter – as well as **World Health Organization** (WHO; Geneva) guidelines.

Klein said the company decided to create a system for lymph assessment because the lymphatic system is heavily tied to cancer metastases. Lymph nodes are typically the first regions of the human body to be affected by cancer spread.

“There is no other solution like this out there,” he said. “It makes it difficult to get FDA approval. The reason no one has tackled lymph nodes is because they are widespread with very different environments and shapes. You can’t use a simple size criterion.”

The Definiens technology doesn’t ignore RECIST or WHO guidelines. In fact it automatically segments lymph nodes and analyzes their properties according to RECIST and WHO criteria. LymphExpert is able to quantify the volume of lymph nodes and their volumetric changes over time. Definiens reported that accurate and detailed analysis of node volume may allow radiologists to detect metastasizing cancer earlier and more readily evaluate the efficacy of treatment protocols.

Definiens LymphExpert promotes the development of personalized treatments, reducing costs and avoiding unnecessary procedures for better patient outcomes, Klein said.

Although Definiens is the lone provider of this new analytical technology, it’s not alone in the belief that this is the future of cancer diagnosis and staging.

The **Radiological Society of North America** (Oak Brook, Illinois) sponsors the Quantitative Imaging Biomarkers Alliance (QIBA), which advocates for accelerating the development and adoption of hardware and software standards to achieve accurate and reproducible quantitative results from imaging methods. QIBA includes representatives from pharmaceutical companies, imaging manufacturers, imaging informatics companies, government agencies, imaging societies, RSNA leadership and clinical trialists. All of the participants back volumetric CT analysis, Klein said.

“This is a pretty prestigious group of people, able to change the way therapy assessment is done,” he said. “The QIBA goal is to come up with something better than today’s diameter measurements. RECIST will in the future be based on volumetric measurements. There is no doubt the proof will be collected.”

Definiens recently completed a study in partnership with **Merck** (Whitehouse Station, New Jersey) which demonstrated how volumetric insight can provide earlier indications of a candidate compound's efficacy, potentially shortening clinical trials and providing substantial cost savings.

So not only does the Definiens technology have applications in cancer diagnostics, but also as part of drug development.

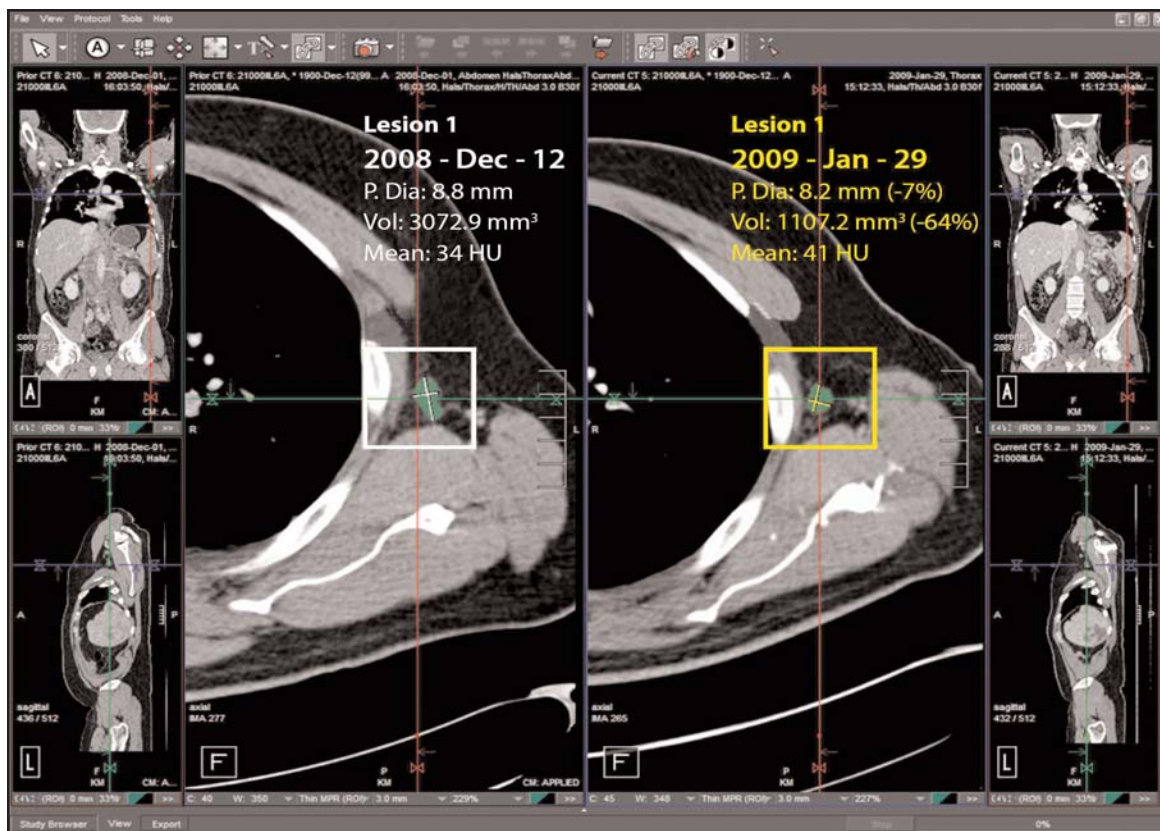
That study has yet to be published, but Klein shared some early results. The retrospective analyses of 10 longitudinal clinical cases of advanced lung cancer compared manual RECIST measures vs. semi-automated volume measures with the Definiens tool. "Compared to RECIST line lengths, the use of volumes clearly shows enhanced sensitivity with respect to determining response to therapy," Klein reported at the **European Society of Radiology** (Vienna) meeting this week in Vienna. "We conclude that it is feasible to perform volumetric analysis efficiently with high accuracy and low variability, even in patients with late stage cancer who have complex lesions."

In four cases, volume was superior over RECIST; in four cases RECIST and volume had equal sensitivity; and in one case RECIST was superior to volume.

Another study reported at ECR was designed specifically to validate LymphExpert against manual human measurements. That study was conducted in cooperation with the **University Hospital of Munich/Grosshadern**. The objective was to assess whether semi-automated analysis could be comparable to a purely manual assessment by human readers. CT data was gathered from 50 cancer patients and analyzed with both RECIST and LymphExpert. Investigators found that the computer-aided quantification of the lymph nodes is comparable to manual measurements. But when using Definiens LymphExpert, the agreement between the comparing investigators increased, shown by a decrease of the standard deviation of the measurement differences from 2.34 mm to 1.15 mm.

Moving forward, Definiens intends to more fully automate the technology.

"We've started with something semi-automatic, which fits with market expectations," Klein said. "The market simply doesn't believe in fully automatic solutions. But the degree of automation will increase over time and we will have a solution that will be fully automatic. We already have an early version of that which produces beautiful images. We strongly believe that's where the future is." ■



Screenshot of Definiens LymphExpert showing a Side-by-side comparison over time of an analyzed lymphnode. A 7% change in the short axis of the lymph node caused a change of 64% in volume.