New imaging technique could ID additional ovarian tumors not visible to surgeons' eyes

15 June 2016

A newly devised tumor-specific fluorescent agent and imaging system guided surgeons in real time to remove additional tumors in ovarian cancer patients that were not visible without fluorescence or could not be felt during surgery.

The study is published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, by Alexander L. Vahrmeijer MD, PhD, head of the Image-guided Surgery group in the Department of Surgery at Leiden University Medical Center in the Netherlands.

"Surgery is the most important treatment for ovarian cancer, and surgeons mainly have to rely on their naked eyes to identify tumor tissue, which is not optimal. Near infrared (NIR) fluorescence imaging is a novel technique that may assist the surgeons to improve visualization of tumors during surgery," Vahrmeijer said.

Philip S. Low, PhD, from Purdue University, and colleagues developed a new fluorescent agent, OTL38, which is a conjugate of NIR fluorescent dye and a folate analog that binds to folate receptor-alpha (FR?). Vahrmeijer and Jacobus Burggraaf, MD, PhD, from the Centre for Human Drug Research in the Netherlands, studied OTL38 for the first time in humans. According to Vahrmeijer, FR? is expressed in more than 90 percent of ovarian cancers but in relatively low levels in some normal tissues.

The researchers first conducted a randomized, double blind, placebo-controlled clinical trial to assess the tolerability and pharmacokinetics of OTL38 in 30 healthy volunteers. This allowed them to rapidly determine the optimum dose range and time window for intraoperative imaging in patients with ovarian cancer, Burggraaf explained.

Next, under the supervision of gynecologist Katja Gaarenstroom, the researchers tested OTL38 in 12 patients with ovarian cancer. In addition to measuring tolerability and pharmacokinetics, they studied whether OTL38-guided surgery resulted in the detection of more tumors that were not visible or palpable during surgery.

The researchers found that OTL38 accumulated in FR?-positive tumors and metastases, and enabled the surgeons to remove an additional 29 percent of malignant lesions (confirmed by pathological examination of the resected tumors) that could not be identified with naked eyes and/or palpation.

This was a small, exploratory study, and was not designed to estimate the sensitivity and specificity of the imaging method. A larger study to address this, as well as other fluorescent agents for other tumor types that do not express FR?, are being planned, Burggraaf added.

Author Comment: "In our study, using a tumor-specific fluorescent agent and a dedicated imaging system, a fluorescent signal was detected in tumors in real time during a surgical procedure for ovarian cancer called cytoreduction. This allowed resection of additional tumor lesions that were not visible to the surgeons' naked eyes," added Vahrmeijer. "Although more research is needed, this is hopefully the first step toward improving the surgical outcome of cancer patients."

"The main advantage of NIR light is that it can penetrate tissue in the order of centimeters, allowing the surgeon to visualize tumors underneath the tissue surface that can be detected using a dedicated imaging system," he explained.

"Our unique approach using a mixed population of healthy volunteers and patients allowed us to rapidly determine the optimum dose and time window for intraoperative imaging," Burggraaf said. "The success of this study was only possible with the close collaboration between several academic and industry partners."

"A limitation of this study is that we cannot say yet what the impact of our findings is on cure or survival of the patients. It is reasonably plausible to assume that if more cancer is removed the survival will be better. However, long-term follow-up studies need to be performed in large patient groups to prove such effects," Vahrmeijer noted.

Provided by American Association for Cancer Research