DLP® technology's pivotal role in O_2view's versatile medical projection / illumination device

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ABSTRACT

Information is presented as to the design of a versatile pattern light projection device that has been essential in the development of the Artemis Broad Spectrum Vision System for imaging of spatial tissue oxygen-saturation measurement as well as of near infrared fluorescent-labeled tumors to facilitate their surgical removal. The combined technology for molecular imaging (Artemis Camera) and image-guided projection of light (Artemis DMD-Projection System) is of significant benefit for various clinical applications. In case of tissue oxygen measurements, the application of illumination patterns of specific near-infrared light and concomitant read out of reflected light from non-illuminated areas theoretically will reveal information from deeper structures. As regards tumor surgery, photodynamic therapy for elimination of tumor tissue is the most exciting and even more demanding, in that the areas to be illuminated perfectly have to match the areas where cancerous tissue is detected. Several performance criteria had to be met for the projection system: mixing wavelengths from different light sources via a 3-channel prism; apochromatic from 430 to 1,000 nm; the projector's zoom-function to follow the Artemis camera zoom settings; the angle of projection to adapt to the full working distance range; and the integration of O_2view´s custom camera controls with the DLP-chip.

Keywords: Artemis, broad-spectrum imaging, DLP, illumination, medical camera system, molecular imaging, photodynamic therapy, surgical oncology

INTRODUCTION

In 2007 and 2008, Artemis was developed as a medical device to quantitatively and qualitatively reveal spatial tissue oxygen-saturation information, important for surgical procedures in general and cardio, reconstructive and trauma surgery in particular. Many enquiries with potential users revealed an absence of interest in this tissue oxygen visualization technology. An application breakthrough came in late 2008 when surgical oncologists displayed their interest in our technology. Using non-invasive imaging technologies like CT, MRI and PET, cancer can be detected much earlier and the tumor can subsequently be removed using minimally invasive techniques or by open surgery. It is of great importance that during surgery the tumor is completely removed with sufficient tumor-free margin. Whilst operating, however, it is extremely difficult to discriminate between tumor and normal tissue. Identification of lymph node metastases is also hard while operating. If, under imaging, intra-operative identification of tumor-free margins and local (lymph node) metastases is possible, and their subsequent radical removal, the life expectancy of cancer patients will be greatly improved.

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A promising development in this area is the use of near infrared-fluorescence (NIRF) imaging. Fluorescent molecules are coupled to antibodies or other substances that specifically will bind to tumor tissue, making real-time visualization of tumor tissue possible during surgery. Tumor cells in the cutting edge, or in lymph nodes, can thus be made visible with high precision and sensitivity. This has been demonstrated using small animal tumor models[1], *e.g.*, using micro-CT (figure 1, left) but also in large animals using experimental NIRF camera systems. Various clinical trials currently are in progress to assess the safety and efficacy of NIRF-probe imaging in humans.

Artemis, with minor adaptations of the optics and camera chips concerned, will be used in the operating room for the visualization of near-infrared labeled tumor tissue, thereby greatly facilitating successful surgical removal of tumor tissue and disseminated disease. For this application, the purpose of the projection system is to provide sufficient amounts of excitation light to the tumor and /or lymphatic tissue in order to make it light-up.

A step further, making full use of the capabilities of the DLP®-technology, is for application in Photodynamic therapy. Photodynamic therapy is a medically approved treatment consisting of local or systemic administration of a photo-reactive compound that can be activated by light[2]. Some photo-sensitizers preferentially accumulate in tumor cells. Light activation of the photo-sensitizers leads to the generation of reactive oxygen species resulting in tumor cell-death, rapidly eliminating local tumors, resulting in cure of early disease and palliation of advanced disease (figure 1, right). Photodynamic therapy compounds exist that can be visualized and activated by using light of different wavelengths. Imaging systems are preferred that combine technology for tumor-localization during surgery and image-guided delivery of activation light for the destruction of tumor tissue that has not been surgically removed. To the best of our knowledge, the Artemis Broad Spectrum Vision System is the first medical device combining these key features. This paper provides information as to the design of the Artemis system in general and of the light projection device in particular.

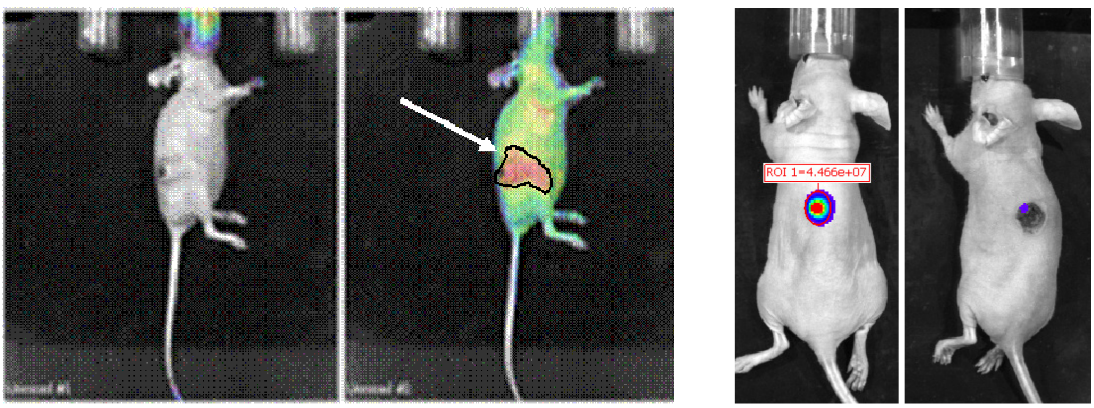

Figure 1: Micro-CT scans. Left: Tumor-margin indicated by Bremachlorin uptake. Right: Tumor progression and regression measured by bioluminescence imaging of cancer cells expressing luciferase. 2 Days after Photodynamic therapy the tumor is almost completely eradicated. The photo-sensitizer Bremachlorin was provided by A. Reshetnickov of Brema Pharma International B.V., the Netherlands. Results made available by C. Löwik, P. van Driel and I. Que of LUMC.

MATERIALS & METHODS

For stereoscopic display the camera of the Artemis Broad Spectrum Molecular Imaging System (O_2view) has two optical zooms (Optec), each with a 5-channel prism in the back-end for the pixel-to-pixel combined visualization of specific contactless clinical observations in visual (VIS) and near-infrared (NIR) light. Light collected by the optical zoom is diffracted by the 5-channel prism into red, green, blue, NIR1 and NIR2 and individually captured by 5 CCD image sensors (Sony ICX285) that are aligned with a maximum misalignment of ¼ of a pixel (Optec). With a spatial resolution of 1,280 × 1,024 at 10 bits / pixel and five image sensors, both 5-channel cameras generate over 150 frames per second in parallel. Because of this large amount of information a scalable processing interface board is used (Eagle-1000, Quest Innovations). Using a Digital Micro-mirror Device (DMD 0.7 XGA 12^o; DLP®, Texas Instruments Incorporated) in combination with a 3-channel projector zoom system (Optec), light from various light sources (high power LEDs 11A1-HW-30 from Roithner Laser Technik GmbH for white light and IQ4A700(785-700)FC-100um-5m laser from Power Technology, Inc. for monochromatic 785 nm light, 725 mW maximum output) is projected onto the patient for diagnostic and therapeutic purposes in patterns that might be specified and guided on the fly by images obtained from the Artemis camera. In addition to this, light for general illumination can also be provided by three Schott KL 2500 LCD external lamp houses by means of a dedicated ring light. See figures 2 and 3 for a render of the Artemis camera and a photograph of the complete system, respectively.

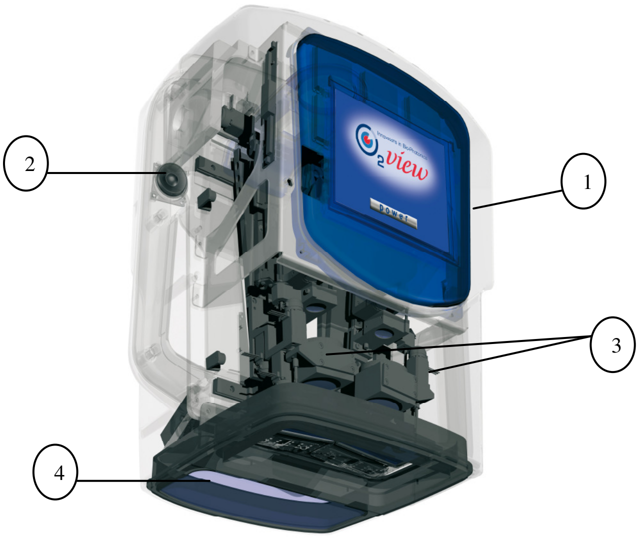

Figure 2: Render of the Artemis Broad Spectrum Molecular Imaging camera showing front part with (1) TFT touch screen, (2) manual controls, (3) left and right automated zooms, (4) ring light. The Artemis projector / illuminator in the back, is not seen. Copyright O_2view B.V.

Figure 3: Photograph of the Artemis Broad Spectrum Molecular Imaging System. Copyright O_2view B.V.

RESULTS

For 2-dimensional qualitative oxygen-level measurements, (oxy) hemoglobin reflective-signals with following wavelengths will have to be acquired simultaneously: red (660 nm), NIR1 (940 nm) and NIR2 (810 nm). Proof of principle of contact-less tissue oxygen-saturation measurement was published by Wieringa *et al.* in 2005[3] according to proprietary technology[4]. For most accurate spatial oxygenation measurement, (near-) perfect pixel-to-pixel alignment of the information simultaneously coming from the three camera chips is essential. In order to provide the user also visual information in full color, it was decided by O_2view in 2008 to build-in a 5-channel prism, designed by Optec S.p.A. This prism with appropriate dichroic coatings separates incoming light into red, green, blue, NIR1 and NIR2 frequencies. Because of its potential applications during surgery, the Artemis camera was designed as a binocular, with auto zoom, auto iris and auto focus. Electronic components for the control of operation of Artemis as well as the FPGA processor boards for on the fly image-data processing were designed by Quest Innovations B.V.

During his research, Wieringa *et al.* pointed out that in theory it is advantageous not to acquire reflected light from areas that are directly illuminated (so-called 'illuminated spots') but from areas that are not illuminated ('dark spots') that are sufficiently close to the illuminated areas[5]. The relative contribution of photons coming from deeper located tissues to the image increase, by acquiring light from dark spots, because disturbing direct-reflected light is not collected. Increased depth of penetration up to 10 mm seems feasible, which is important for revealing hidden structures.

In co-operation with Optec, a dedicated light projection / illumination device was developed for Artemis in order to provide dedicated patterns of 'illuminated spots' and 'dark spots' on the patient's tissue, e.g. checker-board patterns. Figure 4 left, illustrates its position inside the Artemis Camera. For illumination, sources providing various frequencies of light (from 430 – 1,000 nm) are optically coupled to a dedicated 3-channel dichroic prism for mixing the various wavelengths and collimating light into one output axis. See figure 4, right. The output light is collimated onto a Digital Micro-mirror Device to provide for controlled lighting patterns. The design also includes focusing elements and a pinhole for optimal definition of the light bundle coming from the DMD and to avoid ghost images. Next, in the optical path, a tilt-able mirror is placed to continuously adjust the light bundle with the position of the object plane as seen by the Artemis camera. Finally a zoom lens is included, capable of focusing at different distances and fields of view, projecting the light bundle onto the object plane.

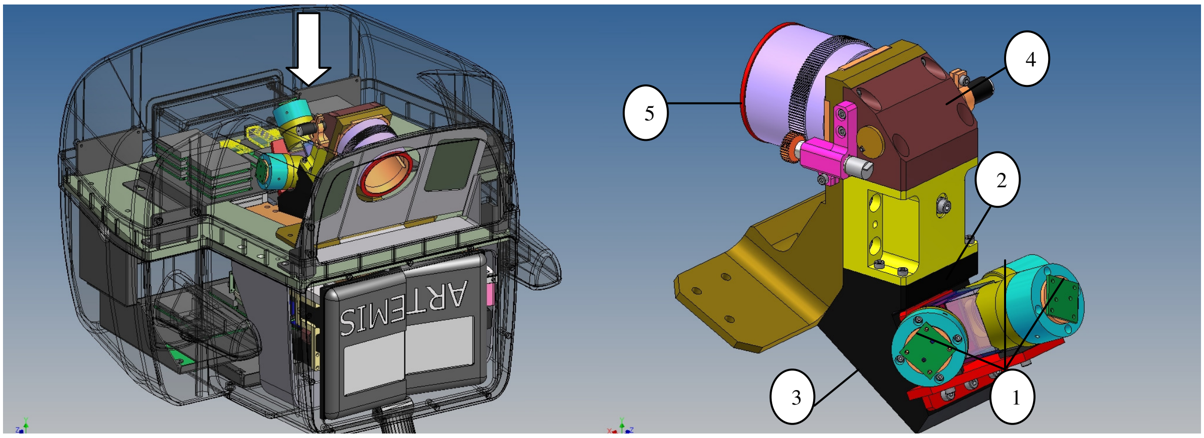

Figure 4, left: Render of the back part of the Artemis camera showing the projection / illumination device inside (arrow). Right: Render of the projection / illumination device assembly, showing 1 = LEDs and / or optical connections for lasers; 2 = 3-channel prism; 3 = location of DMD; 4 = location of tilt-able mirror; 5 = zoom system. Copyright Optec S.p.A. & O_2view B.V.

In order to meet various technical claims, prototypes of stand-alone light projection / illumination devices were tested as to mixing wavelengths from different light sources, optics being apochromatic and the projector's zoom-function to follow the Artemis camera zoom settings. The Full Field Spot Diagram method for ray tracing through the projection / illumination device was used.

Footprints were obtained from individual 1 and 2 mm diameter LEDs with wavelengths of 480, 546, 644, 820 and 910 nm as well as from a VIS – SWIR pass-through (400 – 1,000+ nm range). Projector zoom working distances of 435 and 480 mm were applied, representing 1x- and 4x-zoom magnification. Light coming from the individual LEDs was converted into five point sources: one in the middle and one for every corner. Spot diagrams thus obtained were printed and analyzed. See figure 5 for a representative sample. Results showed that in the image plane the projections of all selections of three sources well overlapped for the entire 480 – 910 nm range and that the system is almost apochromatic. The light projection / illumination device zoom function was able to follow the zoom settings of Artemis.

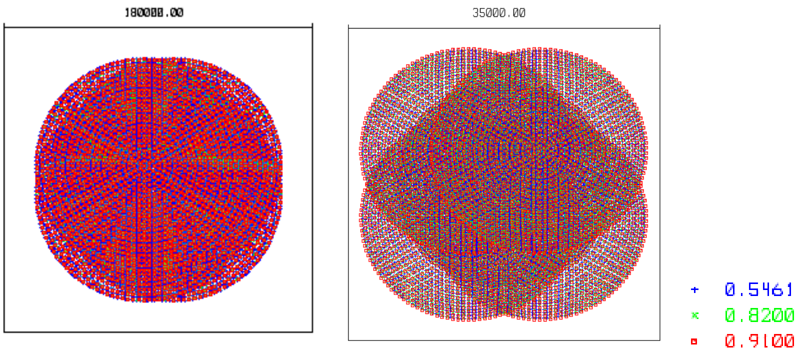

Figure 5: Full Field Spot Diagrams of three 1 mm LEDs at 1x (left) and 4x (right) zoom, demonstrating overlap of light coming from the 546, 820 and 910 nm LEDs. Copyright Optec S.p.A.

DISCUSSION AND CONCLUSIONS

The Artemis Broad Spectrum Molecular Imaging System was initially designed for the visualization of spatial tissue-oxygen saturation distribution for surgical procedures. More recently its clinical potential for the identification of NIRF-probe labeled tumor tissue for (open) surgical oncology procedures has been recognized. Despite the lack of interest in our tissue-oxygen saturation measurement technology from a general surgery point of view, the potential of the Artemis technology to also provide spatial information as to the oxygen-consumption[6] and vascularization[7] for the detection of tumor tissue is perceived by the oncologist as an added value to NIRF-probe imaging for the identification of tumor tissue during surgery.

In order to have sufficient light for NIRF-probe imaging, but also to be able to provide specific geometrical patterns of light in order to obtain information from deeper structures, a versatile pattern light projection / illumination device has been constructed for part of the VIS – NIR spectral region. It is concluded that projections of the sources in the image plane well overlap for the entire 480 – 910 nm range, that the system is almost apochromatic and that the light projection / illumination device zoom function is able to follow the zoom settings of Artemis. In early 2010, following full integration of the light projection / illumination device into the Artemis camera, in a co-operation with Quest Innovations and Optec, the angle of projection to adapt to the full working distance range and the integration of O_2view´s custom camera controls with the DLP-chip will be investigated, the latter investigation also to validate image-guided pattern projection.

The current design of Artemis has been optimized for the visualization of indocyanine green for intra-operative fluorescent imaging of sentinel lymph nodes (in breast cancer); the first clinical data are expected soon. Due to the versatility of optical components and DLP/projector/light source, Artemis can be customized to meet all requirements in the 400 – 1,000+ nm range for a variety of (pre-) clinical applications, both from a medical imaging and application-dependent light projection point of view.

Besides mathematically-derived illumination patterns like checker-board patterns for obtaining deeper tissue signals, the versatility of the DLP-chip will make it also possible to illuminate only those locations were the Artemis camera has detected the near-infrared signals from NIRF-labeled tumor tissue. Currently O_2view, in co-operation with the Leiden University Medical Center, Leiden, the Netherlands, is exploring in animal models the potential of this technology for the simultaneous visualization and activation of photo-sensitizers (e.g. visualization in the 680 – 720 nm range; activation with 662 nm).

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