“Intra-Operative Assessment of Tumor-Resection Margins”

2-3 July 2014, Erasmus Medical Center “Centrum Locatije” Lecture Hall 3
Wytemaweg 80, Rotterdam, The Netherlands

www.epic-assoc.com/events

Pre-operatively, many imaging techniques are available that help a surgeon in planning a tumour resection procedure. This is in stark contrast with the situation in the operating room where the surgeon has to rely on his eyes and hands. As a consequence many resections are inadequate (not all tumour removed, or with a margin smaller than intended). A recent detailed retrospective survey of head and neck cancer procedures at Erasmus-university Medical Centre Rotterdam and Leiden University Medical Centre even showed that 85% (!) of procedures resulted in inadequate resections. Many other tumour resection procedures have high rates of inadequate results. Surgical success rates in terms of complete tumour resection must improve.

Optical techniques such as fluorescence imaging, NIR imaging, and optical spectroscopies (a.o. Raman spectroscopy) can be used to provide detailed tissue classification in real-time. Moreover the photonics technologies on which they are based are highly suitable for deployment in the operating room. There is much research activity in this field.

Photonics-based technologies offer great opportunities to provide the surgeon with real-time information during a procedure. The clinical need is undisputed.

The participants will represent medical doctors, researchers pursuing image-guided and optical spectroscopy-guided surgery, small and large companies able to offer suitable technologies.

The objective of the workshop is to obtain a reasonable understanding of what technologies are most suitable for what applications and in what timeframe they might become available:

- develop a common understanding of the exact needs and requirements of surgeons
- constraints and challenges
- document a roadmap on what technologies are currently available and what approaches should preferably be followed to develop and introduce photonic technologies in the operating room

Speakers are to present the clinical and technological state-of-the-art, advantages and disadvantages, implementation problems and hurdles, what is still needed to clinical validation, etc ...

Missed the last EPIC Biophotonics Workshop? See a summary video on www.youtube.com/watch?v=8yDrd24Um4I
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Different tumors will require different approaches, and there will be a role for a wide variety of photonic technologies. The meeting will offer an opportunity for a fruitful exchange in a collaborative atmosphere.

**Workshop objectives:**

- **Clinicians** will inform technology researchers and photonic companies about:
  - the real down-to-earth clinical problems during oncologic surgery
  - the problems surgeons run into and where do they need help
  - the requirements for intra-operative technology (functionality, workflow, cost (including additional labour), ...). What are no-no’s, and what is acceptable?

- **Researchers & Industry** will present the potential of photonic technologies for intra-operative use

  - Together develop a realistic picture of the feasibility of introducing photonic technologies into the operating room: time-to-clinical-products, cost, complexity, expertise level required, fit in workflow.
    - which information can photonics based technology provide?
    - which development steps are still needed
    - realistic prediction of time to clinical evaluation/validation/product development
    - envisioned regulatory hurdles
    - estimated cost & cost-development
    - ..... 

**Technologies to be presented:**

- Optical coherence tomography
- Raman spectroscopy
- Non-linear microscopy (CARS, SRS)
- Diffuse reflection spectroscopy
- Fluorescence labeling
- Cerenkov Luminescence imaging
- Thz imaging
- Wide Field 2-photon microscopy
- Fluorescence lifetime imaging
- ...

**Clinical problems to be addressed:**

- tumor resections (brain, breast, head & neck, prostate, ...)
- % of inadequate resections
- clinical consequences
- additional cost to healthcare
- ...

EPIC events are known to enhance networking opportunities. At the biophotonics workshop, experts from different disciplines will have a chance to meet and interact: doctors, medical equipment suppliers, photonic components suppliers, integrators and system manufacturers.
Programme

Wednesday 2 July 2014

08:15  Shuttle from SS Hotel to Erasmus Medical Center “Centrum Locatie” Lecture Hall 3, Wytemaweg 80

08:30  Welcome and Registration

09:00  Opening Remarks
  - Carlos Lee, Director General, EPIC – European Photonics Industry Consortium
  - Gerwin Puppels, Chief Technology Officer & Managing Director, RiverD International

Session 1: Clinical Problem Definition
Session Chairs: Robert Baatenburg de Jong & Jose Hardillo, Erasmus-University Medical Center

09:15  Introduction - Future of Surgery
Robert Baatenburg de Jong & Jose Hardillo, Erasmus-University Medical Center

From the evolution of vision in the earliest stages of life, to the primitive forms of imaging in the medieval era, technologies have now culminated into high standards of state-of-the-art imaging modalities. Currently, we are on the verge of the next step: Optical Imaging. Optical imaging comprises e.g. Raman spectroscopy, fluorescence and reflectance spectroscopy. Optical Imaging allows for real-time imaging, up to the cellular and even functional level. When applied in the operating room, optical imaging potentially enables in vivo tissue characterization and evaluation of resection margins: Optical Image Guided Surgery. This promising development is the focus of this workshop.

09:45  Breast cancer surgery
Linetta Koppert, Surgeon, Erasmus Medical Center Rotterdam

Oncological breast surgeons discuss with their patients whether a breast amputation or breast conserving should be planned in order to resect the cancer. They aim for breast conserving surgery when possible with an anticipated good aesthetic result and with free resection margins. Radicality of resection margins cannot always be achieved however and here is room for improvement. When a breast cancer is not palpable the tumor needs to be preoperatively localized for the surgeon. A new localisation technique for non-palpable tumors will be presented.

10:10  The Image Guided Urologist (Prostate cancer surgery)
Martijn Busstra, Urologist, Erasmus Medical Center Rotterdam

Urologists are surgeons that are specialized in the removal of tumors involving the urinary tract. Cure requires radical surgery but still the aim is to diminish collateral damage. Pre-operative imaging by MRI scanning is not sufficient to reach this goal. We need imaging techniques during surgery that can guide us through the operation. Robotic surgery is mostly used by urologists and it offers a promising platform for image guided surgery. In this workshop an experienced robotic urologist will give an overview of current operative techniques and give an impression of what is needed to improve the quality of oncologic urologic operations

10:35  Coffee Break

11:05  Oncological surgery through the eyes of the pathologist
Senada Koljenović, Pathologist, Erasmus Medical Center Rotterdam

The diagnosis and grading of cancer is made by the pathologist. The treatment of choice is most often surgical resection of the tumor. Complete removal is crucial for best patient outcome. Decisions on the necessity for adjuvant radiotherapy and/or chemotherapy are a.o. dependent on the resection margin assessment. During surgery, the pathologist macroscopically evaluates resection margins of the specimen, often followed by microscopic evaluation of frozen tissue sections. This first
assessment provides immediate feedback to the surgeon. Unfortunately, intra-operative evaluation allows inspection of only a very small portion of the resection margins and is time consuming. To make sure the whole tumor is resected, all surgical margins should be assessed during the operation.

11:30 Panel discussion-wrap up clinical problem definition
Facilitator: Fokko Wieringa, Senior Scientist Medical Equipment, TNO

12:00 Lunch

Session 2: Photonics Solutions
Session Chair: Juergen Popp, IPHT

13:00 Intra-operative terahertz probe for detection of breast cancer
Alessia Portieri, Senior Scientist, TeraView

A Terahertz intra operative scanning probe has been developed by TeraView Ltd. for medical use. The probe is capable of acquiring THz images during breast surgery to distinguish between benign and malignant breast tissue, thus assisting in obtaining complete surgical excision of tumors. Initial ex-vivo tests have been carried out using the system located in Guys and St Thomas’s Hospital in London. Initial findings of this study are discussed in this paper.

13:20 Optical Coherence Tomography as a tool to determine non-melanoma skin cancer margins prior to surgery
Daniel Woods, Accounts Development Manager, Michelson Diagnostics

OCT is a non-invasive, non-ionising, real time technique that visualises tissue to a depth of 2 mm at 7.5 μm resolution. Pivotal level-1 trials have shown OCT to have excellent sensitivity and specificity in the diagnosis of BCC. Clinical early adopters have demonstrated a dramatic reduction in average stages during Mohs surgery in Germany. This talk would outline the opportunities and challenges, both technical and commercial, to wider adoption.

13:40 From fluorescence imaging for surgery with Fluobeam® to future fluorescence and Robotic Minimally Invasive Surgery
Francis Glasser, Business Development Manager "Imaging systems" & Philippe Rizo, Engineer, CEA-LETI

ICG fluorescence is used on a daily basis during flap surgery and hepatobiliary surgery. This technique is about to become a standard approach in lymphatic surgery and in some site on breast sentinel lymph node biopsy. Imaging devices such as the Fluobeam® from Fluoptics allow to detect pMol of ICG which correspond to very low amount of fluorescence. This kind of sensitivity is compatible with the imaging of tumors labeled by a specific probe. Fluoptics tested the Fluobeam® on natural tumor (fibro sarcomas, breast cancer and ovarian cancers) on large animals. The results show that the next challenge is to bring the molecules on the bedside. This work is ongoing and few companies are initiating clinical tests on open surgery. Translating this technique to laparoscopy surgery (minimally invasive surgery) will be performed in two steps. First the device will be developed for ICG indications where the fluorescence signal is high: cholecystectomy, control of anastomosis, lymph node mapping and biopsy during prostatectomy. Then it will be optimized to reach the level of sensitivity required to perform tumor margin detection. In this presentation we will provide an overview of the results obtained in open surgery with the Fluobeam® on tumor detection and on ICG imaging. Then we will describe the imaging device dedicated to minimally invasive surgery.
14:00 Lightpoint Medical
Ian Quirk, Director of Clinical and Regulatory Affairs, Lightpoint Medical

Ian Quirk oversees Lightpoint’s clinical and regulatory activities. Ian has more than 20 years of experience in the medical device industry, and has led multiple successful clinical studies and market approvals, in US, EU and beyond. Before joining Lightpoint, Ian was the Worldwide Director of Clinical and Regulatory Affairs at Ranier Technology. Previously, he held clinical, regulatory and quality director roles at Cardiak and Lombard Medical. Ian holds an MSc in Evidence-Based Medicine from Oxford University, a BSc (Hons) in Chemistry from Kingston University, and is currently reading for an LLB at the University of London.

14:20 Water, water everywhere …. intra-operative assessment of tumor resection margins by Raman spectroscopy
Gerwin Puppels, Erasmus MC, Center for Optical Diagnostics & Therapy & RiverD International

Raman spectroscopy is a non-destructive optical technique which provides detailed information about the overall molecular composition of a tissue. The technique does not require reagents, labels, or other contrast enhancing agents. Tumor tissue and surrounding healthy tissue differ in their molecular composition and can therefore be distinguished. Spectrum analysis can occur in real-time. The presentation will highlight the current status and the path to clinical implementation.

14:40 Combined autofluorescence and Raman spectroscopy for assessment of tumor resection margins during Mohs’ micrographic surgery
Ioan Natingher, Associate Professor, University of Nottingham

One of the main challenges in cancer surgery is ensuring that all tumour cells are removed during surgery, while sparing as much healthy tissue as possible. Raman micro-spectroscopy is a powerful technique that can discriminate between tumours and healthy tissues with high accuracy, based entirely on intrinsic chemical differences. However, raster-scanning Raman micro-spectroscopy is a slow imaging technique that typically requires data acquisition times as long as several days for typical tissue samples obtained during surgery (1x1 cm²) - in particular when high signal-to-noise ratio spectra are required to ensure accurate diagnosis. However, auto-fluorescence images can be used to obtain information regarding the spatial features of the tissue, which then can be used to generate sampling points for Raman spectroscopy. This technique reduce drastically the number of Raman spectra required for diagnosis, thus allowing diagnosis of basal cell carcinoma in tissue samples excised during Mohs micrographic surgery faster than frozen section histopathology, and two orders of magnitude faster than previous techniques based on raster-scanning Raman microscopy.

15:00 Diffuse reflectance spectroscopy (DRS) for identification of breast cancer in lumpectomy specimen
Lisanne de Boer/OIO/Philips/Nederlands Kanker Instituut – Antoni van Leeuwenhoek ziekenhuis

Breast-conserving surgery (BCS) is an effective treatment provided adequate surgical margins can be obtained but even in highly specialized cancer centers often over 10% of BCS patients are left with a positive resection margin after initial surgery. We investigated whether DRS based on altered spectroscopic properties in malignant tissue can provide guidance in differentiating benign from malignant tissue. Using an optical probe, spectra between 400 and 1600nm of macroscopically malignant, benign and borderline tissue were obtained. Comparing the shape of the tumor spectra with the benign spectra clear differences were seen, especially in the 1000-1200nm wavelength region where fat and water are the dominant absorbers. DRS was able to distinguish benign tissue from malignant tissue based on fat and water content. In the transition zone around the tumor the fat and water content gradually changed suggesting DRS could help guiding surgeons in recognizing the tumor border.

15:20 Coffee Break
Session Chair: Gerwin Puppels, Chief Technology Officer & Managing Director, RiverD International

15:50 Video-rate structured illumination microscopy for high-throughput intra-operative prostate pathology
J. Quincy Brown, Ph.D., Assistant Professor, Department of Biomedical Engineering
Program Member, Tulane Cancer Center, Tulane University, New Orleans

Current intra-operative pathology techniques such as frozen section analysis are of limited value for detection of residual cancer on ex vivo tumor resection margins, especially in organs with large resection specimens such as the breast, prostate, thyroid, and soft tissue sarcoma. The large size of the specimens poses a sampling challenge (where to cut?) as well as a technical challenge (how to rapidly cut enough sections to comprehensively assess the margin?) for traditional pathology methods. An intra-operative ex vivo pathology imaging tool could provide value, if it could be used on fresh intact specimens, and possessed the required balance between speed, area throughput, histological contrast, and resolution. In order to address these requirements, we are developing video-rate structured illumination microscopy, combined with topical fluorescent staining, as a means to rapidly obtain gigapixel, optically-sectioned, "histological landscapes" of entire ex vivo margin surfaces in intra-operative timeframes. In this presentation we will share results of this high-throughput technology for diagnosis of cancer in intact prostate core needle biopsies, and for acquisition of "virtual whole mount" images from intact whole prostate excisions.

16:10 Multimodal imaging: A powerful approach for modern Biophotonic research
Juergen Popp, Director, Leibniz-Institute for Photonics Technologies, Germany

Optical imaging technologies such as Raman imaging have proven to be a valuable tool in medical diagnostics. The often long acquisition times for Raman spectroscopy can be reduced by utilizing non-linear Raman approaches like CARS (coherent anti-Stokes Raman scattering). This approach allows recording Raman images of single characteristic Raman bands in real time. In order to further improve the diagnostic result CARS microscopy can be easily extended by the two other non-linear contrast phenomena second harmonic generation (SHG) and two-photon fluorescence (TPF). In this contribution we will present the development of a compact CARS/SHG/TPF multimodal nonlinear microscope in combination with novel fiber laser sources for use in clinics. The diagnostics potential of this compact multimodal microscope as compared to conventional histopathological images has been demonstrated for the examples of atherosclerosis and cancer.

16:30 Fluorescence lifetime techniques for label-free intraoperative delineation of tumor-resection margins
Laura Marcu, Professor of Biomedical Engineering and Neurosurgical Surgery, University of California Davis

This presentation overviews clinically-compatible time-resolved fluorescence spectroscopy (TRFS) and fluorescence lifetime imaging (FLIM) techniques for tissue diagnosis developed in our laboratory. Studies conducted in patients undergoing surgical removal of primary brain tumors (glioblastomas) and head and neck cancer will be presented. Current results demonstrate that fluorescence lifetime-based measurements can provide useful label-free contrast for intraoperative diagnosis of these diseases.

16:50 Multimodal Wide-Field and High-Resolution Optical Imaging for Rapid and Accurate Delineation of Cancer Margins
Anna N. Yaroslavsky, PhD, Associate Professor of Physics, University of Massachusetts, Lowell

Intraoperative delineation of cancer margins is an important problem in surgical oncology. Very few clinical methods are currently available for the demarcation of benign and malignant tissue during surgery. Several optical techniques, including polarization sensitive optical coherence tomography, wide-field and high-resolution reflectance and fluorescence imaging are capable of cancer delineation and offer complementary information. A multimodal approach has the ability to exploit the strengths of each technique to adequately address the problem of intraoperative cancer detection. The goal of this presentation is to discuss the utility of optical multimodal imaging as a practical tool for rapid, accurate and efficient intraoperative detection of tumor margins. Several combinations of the above mentioned imaging methods will be discussed in the context of clinically relevant delineation of breast, brain, and skin cancers.
17:10 **Fluorescence molecular imaging sustains enhanced cancer visualization in surgery and endoscopy**  
*Pilar Beatriz Garcia Allende, Chair for Biological Imaging & Institute for Biological and Medical Imaging, Technische Universität München and Helmholtz Zentrum München*  
Among the various optical techniques considered for surgical and endoscopic imaging, wide field targeted imaging with near-infrared fluorescence appears to be the most promising approach to shape the future of these clinical procedures. Increased light tissue penetration is obtained by imaging in the NIR range, while an enhanced tumor-to-background ratio is attained by targeted fluorescent agents that provide molecularly specific detection of cancer cells and allow the recognition of otherwise invisible disease biomarkers. An overview of the key developments from our laboratory will be given in the talk, and their potential to shift standard surgical and endoscopic imaging practices is discussed.

17:30 **Optical Spectroscopy for the Assessment of Tumor Resection Margins**  
*Dominic Robinson, Assistant Professor in Optical Diagnostics and Therapy, Erasmus University Medical Center, Rotterdam*  
Wide field fluorescence image guided is performed with the full knowledge that tissue optical properties have a very strong influence on the recovered signals. We have developed methods using point optical spectroscopy that can recover the intrinsic fluorescence (the fluorescence that is unaffected by the tissue optical properties). We are implementing clinical applications of this approach to improve fluorescence image guided surgery with particular focus to measuring tissue optical properties and intrinsic fluorescence in and outside the surgical margins.

17:50 **End day 1**

18:00 Shuttle to SS Rotterdam Restaurant & Hotel. Address: 3 Katendrechtsehoofd 25, 3072 AM Rotterdam  
Dinner: Entrance access number 3. Hotel reception: Entrance access number 1.

18:30 Reception

19:30 Dinner at SS Rotterdam “Sky Room”

**Thursday 3 July 2014**

08:15  Shuttle from SS Rotterdam Hotel to Erasmus Medical Center “Centrum Locatie” Lecture Hall 3

08:30  Welcome Coffee

**Session 3: Photonics in surgery - implementation: status, hurdles, challenges**

*Chair: Kees Verhoef/Rob Baatenburg, Erasmus Medical Center Rotterdam*

09:30 **Fluorescence Guided Surgery**  
*Alex Vahrmeijer, Image-guided surgery group, Leiden University Medical Center*  
Due to its relatively high tissue penetration, near-infrared (NIR; 700-900 nm) fluorescent light has the potential to visualize structures that need to be resected (e.g. tumors, lymph nodes) and structures that need to be spared (e.g. nerves, ureters, bile ducts). To date, we have performed NIRF guided surgery in over 500 patients in more than 25 approved clinical trials. Many trials were focused on NIR fluorescent sentinel lymph node mapping. Other trials were focused on tumor identification, including rare pancreatic tumors, breast tumors and colorectal liver metastases. We will review the key results from these studies and from recent pre-clinical and clinical studies using tumor targeted contrast agents. Moreover, a clear roadmap for clinical translation of targeted probes will be presented.
09:50 Optical Biopsy with Patent blue V for head and neck cancer imaging
Ingrid Breuskin, Head and Neck Surgery, Gustave Roussy

Limited endoscopic resection of cancer of the pharyngo-larynx provides a good local control of the disease while minimizing sequelae. However, pre-malignant changes and small sizes lesions escape to macroscopic observation. Surgeon has limited tools, to clarify the extent of the tumor and achieve adequate resection, and repeated biopsies are not always possible for small lesions. There is a major interest to evaluate new technologies allowing for the “on line” imaging of tissue abnormalities at the microscopic level during intraoperative procedures. Probe-based confocal laser endomicroscopy (pCLE) uses optical fibers of small diameter that can produce in vivo images of tissue at the cellular level. This technology could be adapted for optical biopsy of head and neck cancer.

10:10 Assessment of intra-operative surgical margins in skin cancer using high-definition optical coherence tomography imaging
André Oliveira, Michael Tripold, Juan Garcias-Ladaria, Edith Arzberger, Rainer Hofmann-Wellenhof
Department of Dermatology – Medical University of Graz. Presented by Frans Dhaenens, Agfa Healthcare

High-definition optical coherence tomography (HD-OCT) was recently introduced allowing the in vivo assessment of skin. HD-OCT is capable of capturing not only slice but also en face images in real time and fast three-dimensional acquisition, enabling the visualization of individual cells. Repeated investigations of the same skin lesion without any tissue alterations are possible. Hence, HD-OCT represents an ideal tool not only for diagnostic purposes in skin cancer, but also as an adjuvant both in non-surgical and surgical treatments. We discuss the utility of HD-OCT imaging in the assessment of margin definition prior to skin cancer surgery. This non-invasive technique may prevent incomplete excisions and expensive, unnecessary repetitive procedures. It may also allow smaller excisions as a sparing tissue method.

10:30 Techniques for maximising extent of resection in patients with malignant glioma
Michael D Jenkinson PhD, FRCS (Neurosurgeon), Consultant Neurosurgeon and Honorary Senior Lecturer
The Walton Centre for Neurology and Neurosurgery, University of Liverpool

Glioblastoma are malignant primary brain tumours with a median survival of 12-14 months. Current treatment involves maximum safe resection, radiotherapy and chemotherapy. During surgery, discriminating tumour tissue from normal brain is difficult, even with modern surgical adjuncts such as image-guidance software, ultrasound and intra-operative MRI. A recent development is the use of ALA to perform fluorescence-guided resection. A phase III study has shown that ALA facilitates complete resection of the enhancing tumour and this prolongs disease-free and overall survival (Stummer 2008). ALA is taken orally by the patient 3-4 hours before surgery, but there is a 5-10% risk of photosensitivity reaction and patients have to be nursed in low light levels for 24 hours. ALA costs £950+vat per patient and is not currently available in routine clinical practice in the UK. Therefore, there is an urgent need for alternative and cheaper methods for accurately detecting tumour tissue during surgery, which will maximise safe resection.

10:50 Coffee Break

11:20 Short company presentations

11:50 Discussion on roadmap to implementation in tumor surgery (break-up in different clinical applications)
Facilitator: Fokko Wieringa, Senior Scientist Medical Equipment, TNO

12:25 EU-Research Funding Priorities
Facilitator: Maurice van den Dobbelsteen, Senior Consultant, PNO

12:45 Lunch and Networking

13:30 Hospital visit for EPIC Members
Participants Information

Ellen Hoogenes, Key Account Manager  Frans Dhaenens, Clinical Research Consultant, HE/IMG Marketing & Sales

**Agfa HealthCare**, a part of the Agfa-Gevaert Group, is a leading provider of integrated IT solutions, state-of-the-art diagnostic imaging and contrast media solutions for hospitals and other healthcare centers. Agfa HealthCare has over a century of healthcare experience related to medical imaging and has been an active player on the healthcare IT market since the early 1990’s. Agfa HealthCare has sales offices and representatives in over 100 markets worldwide.

**Andor** - Colin Coates, Product Manager Imaging and Spectroscopy

Andor Technology (Andor) is based in Belfast, Northern Ireland and operates at the high-value end of the global scientific digital camera market. Andor was setup in 1989 out of Queen’s University in Belfast, and now employs over 400 people in 16 offices worldwide and distributes its products in 55 countries, to a customer base encompassing both the scientific research and industrial communities, in both life and physical science disciplines. The company has grown rapidly, both organically and through strategic acquisition, and is today market leading provider of high performance scientific digital cameras. Along the way Andor has pioneered the development of new and innovative camera technologies, including Electron Multiplying CCD (EMCCD) and Scientific CMOS (sCMOS) cameras. In January 2014, Oxford Instruments, a leading provider of high-technology tools for industry and research, announced the acquisition of Andor Technology. As a result of this acquisition, Andor will continue to focus on growing existing core markets and will spearhead Oxford Instruments strategic expansion into the Nano-Bio arena.

**art photonics** - Viacheslav Artyushenko, CEO

Fiber spectral systems under development and already used in clinics are based on different spectral methods – starting from fluorescence methods like Photo-Dynamic Diagnostics (PDD) of cancer and diffused reflection spectroscopy up to Mid IR absorption and Raman spectroscopy used for label free molecular analysis of tissue or bio-liquids in-vivo. Promising synergy in optimal combination of complimentary spectral methods enables modular design of promising fiber sensors to be used for in-vivo definition of tumor-resection margins. Possible applications of fiber spectroscopy for such in-vivo diagnostics is starting from high end research spectroscopy systems, but should lead to development of low cost fiber sensors required for clinical and ambulatory applications. [www.artphotonics.com](http://www.artphotonics.com)

**BioVolt** - Eric Smith, CEO

BioVolt’s mission is to support the Life Sciences by delivering the next-generation of analytical tools and solutions for use at all points-of-need. In order to achieve this, BioVolt exploits a patented micro-scale optical interferomic platform which implements arbitrary molecular assays with lab-grade performance and unique levels miniaturisation and disposability.
RiverD International develops and brings to market dedicated solutions for unmet diagnostic needs, based on Raman spectroscopic analysis of cells and tissues.

RiverD’s Raman technology platform excels in sensitivity and reproducibility and is readily adaptable to the specific demands of a particular application.

The gen2-SCA family of in vivo skin analyzers provides unique insight into the molecular composition of the skin with high spatial resolution, and enables the study of skin penetration properties of topically applied materials. This technology is in use worldwide by personal care industry, pharmaceutical industry and university medical centers.

The SpectraCell RA Bacterial Strain Analyzer is RiverD's answer to the need for simple high throughput technology for bacterial typing. At the Erasmus MC in Rotterdam the system is in routine use for rapid analysis of potential outbreak situations and for prospective monitoring of transmission of antibiotic-resistant bacterial strains.

We love what we do and we would love to hear from you. Please feel free to contact us for more information or to discuss an idea or application.

Contact:
Gerwin Puppels
Tel:+31-10-7044841
puppels@riverd.com
Bracco is an international Group active in the healthcare sector through Bracco Imaging (Diagnostic Imaging), Pharma (prescription and over the counter drugs), Acist Medical Systems (medical devices and advanced imaging agents injection systems based in Minneapolis, USA), and the Centro Diagnostico Italiano diagnostic clinic in Milan. It has more than 3300 employees and annual total consolidated revenues of over 1,2 billion euros, of which 70% from international sales, and it is present worldwide. In the Research and Innovation area, the company invests approximately 10% of reference turnover in the imaging diagnostics and medical devices sectors and has a portfolio comprising over 1,500 patents. Bracco Imaging is one of the world’s leading companies in the Diagnostic Imaging, it offers imaging agents, injectors and solutions portfolio for all diagnostic application: X-Ray Imaging (including Computed Tomography-CT), Magnetic Resonance Imaging (MRI), Contrast Enhanced Ultrasound, and Nuclear Medicine.

Cambridge Consultants - Cat Fitzpatrick, Senior Engineer, Medical Technology Division
Cambridge Consultants develops breakthrough products, creates and licenses intellectual property, and provides business consultancy in technology critical issues. Solutions cover a range of industries including Cleantech, medical technology, industrial and consumer products, transport and wireless communications. Cambridge Consultants is part of the Altran Group, the European leader in Innovation Consulting.

CHUV - Lausanne University Hospital - Claudio Bruschini, Project Manager
Claudio Bruschini has a dual affiliation with the Nuclear Medicine and Molecular Imaging Service at the Lausanne University Hospital (CHUV) under Prof. J. Prior, and the Advanced Quantum Architectures group under Prof. E. Charbon at the Ecole Polytechnique Fédérale de Lausanne (EPFL). R&D activities of interest to the workshop are centred on the exploitation of single photon solid state sensors (SPADs) in biomedical applications such as low light level imaging, Fluorescence Lifetime Imaging (FLIM) in oncology, novel nuclear medicine instrumentation (e.g. for PET), Raman spectroscopy, superresolution microscopy, and Fluorescence Correlation Spectroscopy. Part of the R&D is carried out with selected external partners as well as within European projects such as MEGAFRAME (completed), SPADnet and EndoTOFPET-US (ongoing).

Ephoran Multi Imaging Solutions - Giovanni Valbusa, Researcher
EPHORAN is a Multi-Imaging Service Company focused on preclinical research and development. The mission of the Company is to study, develop and pursue the application of imaging technologies in preclinical drug research and development. EPHORAN will foster the development of diagnostic tools, reagents and methodologies for experimental imaging.

The workshop is organized by EPIC with the support of RiverD
The workshop is hosted by the Erasmus Medical Center Rotterdam

Erasmus Medical Center Rotterdam - Roeland Smits
Erasmus Medical Center Rotterdam - Clemens Dirven, Medical Doctor, Neurosurgeon
Erasmus Medical Center Rotterdam - Lena Van Doorn, Gynaecologist
Erasmus Medical Center Rotterdam - Stijn Keereweber, Medical Doctor
Erasmus Medical Center Rotterdam - Senada Koljenovic, Medical Doctor, Pathologist
Erasmus Medical Center Rotterdam - Florence Atrafi, Medical Doctor
Erasmus Medical Center Rotterdam - Rob Verdiijk, Pathologist
Erasmus Medical Center Rotterdam - Inês P. Santos, PhD Dermatology Department
Erasmus Medical Center Rotterdam - Elisa Barroso, PhD CODT Group, Maxillofacial Department

Fraunhofer PAMB (Automation in Medicine and Biotechnology) - Nikolaos Deliolanis, Group Leader
Fraunhofer PAMB is a newly established Project group of the Fraunhofer Society focusing on applied R&D on Automation in Medicine and Biotechnology. Fraunhofer PAMB is located inside the University Hospital in Mannheim - the teaching affiliate of the University of Heidelberg, and is in close collaboration with the medical community. The Biomedical Optics group works in the development of novel optical measurement technologies for the biomedical applications market to become the next generation of products, such as surgical microscopes and endoscopes, which are capable of real-time multispectral imaging of multiple fluorescent agents simultaneously with color images.

Guy's Hospital/King's College London - Maarten Grootendorst, Research Fellow
Guy's Hospital/King's College London is a university located in London. The clinical partner of King's College London is Guy's and St Thomas' NHS Foundation Trust. As part of King's Health Partners, an academic health sciences centre, we're pioneers in health research, and provide high quality teaching and education. This partnership helps us provide the latest treatments for you alongside the best possible care.

Hamamatsu Photonics is a worldwide leading manufacturer of opto-electronic components and systems. Among others we offer sensors and systems for spectroscopy (including ultra fast), scientific-grade cameras, beam monitoring solutions, photon counting detectors and systems, photomultipliers, photodiodes, IR detectors.

www.hamamatsu.com
with LioniX the www.lionixbv.nl Gustave Roussy, located in the south of Paris, is a key actor on the European and international oncology scene. The institute applies a global approach to cancer, employing multidisciplinary teams to care for each patient and define by a multidisciplinary process the best treatments for them. Every year, the Gustave Roussy medical teams see more than 11,400 new patients, with 149,000 consultations, and treat 44,400 patients. Top level research, conducted at the very heart of the Institute, is aimed at the integration of basic, translational and clinical approaches, so that the results can be applied as quickly as possible for the benefit of the patient. The teaching provided to the students, researchers and practitioners, enables them to bring into practice new developments in cancer treatment, and introduce innovations. The Institute is a driving force in the dissemination of knowledge and training by exporting its working models, its experience and medical expertise abroad. Further, numerous academic partnerships are nurtured with the greatest cancer centers in the world for worldwide research projects. In the Department of Biopathology, the pathologists define the benign or malignant nature of the tissue samples collected from patients by the physicians, which can be biopsies or surgical specimens, through the macroscopic and microscopic study, on histological slides. The aim is to provide to the clinicians a precise diagnosis and others elements for therapeutic decision, such as the quality of the resection limits or metastatic lymph node invasion. The Department of Biopathology collaborates to new optical imaging developments for surgical guidance in oncology, in collaboration with the Department of Head and Neck Surgery and the Imaging and Cytometry core platforms of Gustave Roussy.

KARL STORZ - Norbert Hansen, Project Manager
KARL STORZ is one of the world’s leading suppliers of endoscopes for all fields of application. The family-owned company with its headquarters in Tuttlingen, Germany has 6,700 employees worldwide. With a history that stretches back over 65 years, KARL STORZ is well-known for its innovative and high-quality products. Its range of products has been rounded off with the development of the integrated operating room OR1 and by integrating the field of flexible endoscopy into the various specialties.

Leiden University Medical Center, Dept. Radiology - Jouke Dijkstra, Associate Professor
Jouke Dijkstra, PhD, associate professor Leiden University Medical Center, Leiden, the Netherlands
Department of Radiology, Section Vascular and molecular imaging.
Focus: imaging processing, translational research, optical imaging.

LioniX - René Heideman , CTO and Co-Founder
LioniX is a provider in development and small to high volume production of innovative products based on micro/nano system technology (MNT) and MEMS. Our core technologies are integrated optics and micro-fluidics. Our customers operate in telecom, industrial process control, life sciences and space markets and include OEM’s, multinationals, VC start-up companies as well as research institutions from around the world. LioniX offers design to manufacturing and horizontal integration by partnering with MEMS/MST foundries and suppliers of complementary technologies, such as in (food) biotech/genomics, chemistry/pharmaceuticals and water technology. The combination of micro-fluidics and integrated optics gives LioniX expertise in the emerging area of Lab-on-a-Chip. LioniX has its own clean-room facilities with equipment for the proprietary technology and dedicated test/analysis equipment for integrated optics and micro-fluidic devices.

www.lionixbv.nl
LLTECH - Fabrice Harms, CTO

LLTech is a start-up company dedicated to the development of Full-Field Optical Coherence Tomography (FFOCT) instruments for clinical applications. This proprietary OCT technique provides about 10x better resolution than conventional scanning OCT, typically 1µm in 3D. This feature makes FFOCT one of the best optical biopsy technique targeting intraoperative cancer assessment without the need for any contrast agents. The company already commercializes a FFOCT microscope dedicated to research, and is currently developing both a clinical microscope for intraoperative biopsy assessment, but also a high resolution FFOCT endoscope providing cellular resolution images in depth without any contrast agents (see FP7 project CAReIOCA: www.careioca.eu). Current clinical results using the technique have demonstrated a very good morphology correlation with histology, and some good diagnosis capabilities on a couple of tissue types (prostate, sentinel nodes, etc.)

Giuseppe Solomita, Director International Sales

MAVIG VivaScope Systems. Reflectance confocal microscopy is a non-invasive imaging modality that provides real-time images at cellular resolution down to 200-250µm in vivo. The cellular resolution, also called quasihistological resolution, enables a great correlation with histology. More than 450 publications highlight the high sensitivity and specificity for the diagnosis of BCC, melanoma, squamous cell carcinoma and improved presurgical mapping of lentigo maligna amongst many other skin conditions. In the MOHs surgery setting, the ex vivo VivaScope 2500 allows for the fast examination of excised tissue. Preliminary studies for BCC show a high sensitivity and specificity and tremendous reduction in the time and costs of a MOHs surgery. During the workshop existing results about the use of the VivaScope 2500 in the MOHs surgery setting will be shared and a future outlook provided.

Stephanie Muth, Junior Key Account Manager

Modulight - Sampsa Kuusiluoma, Manager, New Product Introduction, Integrated Laser Solutions

Modulight is an ISO9001, ISO14001 and ISO13485 certified company focusing on design, development and manufacturing of laser diodes and laser systems. Modulight lasers are deployed mainly in medical, industrial, security/defence and display/projection markets. The company provides components and turnkey laser systems with wavelengths range between 405 nm and 1650 nm and power levels up to 100 W along with design and implementation of sub-system level laser integration including cooling, drivers and mechanical design. The products are offered from bare and mounted laser chips to packaged and fibre-coupled lasers and complete turnkey laser systems. The Company has in-house laser diode production facilities and headquarters in Tampere, Finland and a fully owned subsidiary Modulight USA, Inc., based in San Jose CA. www.modulight.com

Multitel - Fabian Dortu, Group Leader Biophotonics

The Biophotonics Group develops and exploits Multitel's know-how for biomedical and industrial biotech applications. The group allies Multitel's know-how in photonic sensor technologies (optical fiber, photonic circuits), new generation light sources (CW and pulsed lasers, supercontinuum), laser processing, automatic image processing and embedded electronics to respond to the automation needs of biotech companies, with a particular emphasis on diagnostic related activities. www.multitel.be/photonics
Ocean Optics - Ruud Niesen, Sales Manager
Ocean Optics, a diversified photonics technology company, is the inventor of the world's first miniature spectrometer (for water research) and is a global leader in optical sensing technologies. Since 1992, Ocean Optics has been developing and manufacturing the highest quality, most innovative products for optical sensing and more. Our systems have been used to discover water on the moon, analyze samples on Mars, detect explosives in Afghanistan, diagnose disease in hospitals, monitor the climate from Mt. Everest, track acidity within our oceans, and measure emissions within live volcanoes.

PNO - Maurice van den Dobbelaar, Senior Consultant
PNO Consultants is Europe’s largest independent grants advisory with 250 staff and over 25 years in operation. We help our clients and partners identify public funding opportunities based on their competencies and objectives and we help define project ideas and put together the consortia. PNO manages the application process and writes and submits the proposal. Most of our staff has scientific and research backgrounds, enabling us to contribute to the scientific content and research planning. PNO also supports its clients during the negotiation, kick-off and management phases of their projects. We also provide a range of innovation management services which can be deployed within regionally, nationally and EU funded projects including creation and management of networking platforms, stakeholder relationship management, market & technology analysis, planning and roadmapping, coordination, surveys, impact assessments, training, business case development and dissemination. PNO raised over €150M in funding for its clients in 2011. [www.pnoconsultants.com](http://www.pnoconsultants.com)

Gerald Lucassen, Technology Manager
Benno Hendriks, Research Fellow

Royal Philips of the Netherlands is a diversified technology company, focused on improving people's lives through meaningful innovation in the areas of Healthcare, Consumer Lifestyle and Lighting. The company is a leader in cardiac care, acute care and home healthcare, energy efficient lighting solutions and new lighting applications, as well as male shaving and grooming and oral healthcare.

Angelo Ferrario, President
Antonio Raspa, EU Projects Manager

Quanta System was founded in 1985 and belongs to the EI. En. Group (a public company listed in the Star segment of the Italian Stock Exchange) since January 2004. The company, divided into three business units (medical, scientific and industrial) is specialized in manufacturing of laser and opto-electronic devices. Quanta System is an important player in the worldwide laser technology market, specialized in 3 scientific fields: Surgery, Aesthetics and Art. They are distinct sectors, united by a common methodological approach which focuses on the quality of life and care for People. Quanta's orientation to innovation is realized into a constant effort to introduce new technologies and equipment which are able to satisfy the most demanding requirements and guarantee the best results to physicians and patients. A value, the one of Research, which is inside the company DNA, and deeply follows the tradition which, since ever, has accompanied Italians, a Population of explorers and great inventors.
Quanta’s successes all over the world confirm the strong push for innovation and the internationalization of Italian projects and technologies. They represent some of the stages into that beauty and health route which is every day explored through systems for Aesthetics and Surgery, always led by the principle: “taking care of people, our masterpieces”.

**TEMATYS - Clémentine Bouyé, Biophotonics Technology and Market Analyst**

Tematys is independent. Our team of highly qualified consultants is committed to provide a very comprehensive understanding on trends, markets and use of photonic technologies and their applications. Our Biophotonics Department is responsible for following the evolution of Biophotonics technologies and markets, from small sensors to big imaging systems. Tematys published of a prospective report sponsored by EPIC on the evolution of biophotonic devices ("Biophotonics Market", April 2013). We plan to release a review of the OCT technologies and markets in summer 2014 and one on microspectrometers for portable analysis devices next winter. [www.tematys.com](http://www.tematys.com)

**TNO** is a Dutch not-for-profit research organization that connects people and knowledge to create innovations that boost the sustainable competitive strength of industry and well-being of society. TNO’s unique position is attributable to its versatility and capacity to integrate knowledge. Across a wide range of technologies, from food & medicine, automotive and aerospace, ICT and defense, TNO supports its customers with the state of the art in technology and applied knowledge. Our fields of knowledge are: applied physics, mechanics, material and process technology, instrumentation, electronics and information science. Projects, both national and international, vary from system development to consultancy. TNO has an impressive track record in leading and contributing to European Framework Programs. Established by law in 1932, TNO presently employs approximately 3500 personnel. TNO is a not-for-profit organization, with an annual consolidated turnover of approximately €550 million. Within TNO, the Van ’t Hoff Shared Innovation Program is a collaborative research program amongst industry, government, hospitals and non-profit health foundations that aims to improve health care using biophotonics-based technologies. [www.tno.nl](http://www.tno.nl)

**Leiden University Medical Center (LUMC)** - Paulien Stegehusi, PhD, Student Surgery and Radiology Department

LUMC is a modern university medical centre for research, instruction and patient care. Its unique research practice, ranging from pure fundamental medical research to applied clinical research, places LUMC among the world top. This enables LUMC to offer patient care and instruction that is in line with the latest international insights and standards – and helps it to improve medicine and healthcare both internally and externally. With more than 7000 staff members, the LUMC focuses on top clinical and highly specialised care: the complex medical issues for which there are often not yet any answers. A considerable portion of the research centres on the translation from fundamental research to its use in patient care (from bench to bedside and vice versa).
Tyndall National Institute - Paul Galvin, Head of Life Sciences Interface Group

The Tyndall National Institute, University College Cork, is one of Europe’s leading centres for Information, Communications and Technology (ICT) research and development. Tyndall is the largest facility of its kind in Ireland. Tyndall, formally known as the National Microelectronics Research Centre, was established in 2004 to provide a critical mass of researchers that would support the growth and development of a smart knowledge based solutions for health, communications, energy and environmental applications. www.tyndall.ie

University of Nottingham - Kenny Kong, Research Associate

The University of Nottingham’s expertise and facilities include III-V epitaxy, nanofabrication, electron beam lithography, surface science, high resolution microscopy, optical and electrical test, microelectronics and micromachining, experimental and numerical studies of optical waveguides, lasers and amplifiers and nano-scale photonic circuits. Theoretical simulation includes direct access to cluster computing facilities. Programmes of research cover photonic integrated circuits at various wavelengths, graphene and spintronic devices, wide bandgap nitride semiconductors and Raman spectroscopy applied to biomedical imaging. Laser materials processing work includes cutting, drilling, cladding, surface melting, heat treatment and additive manufacture. We manufacture and characterise mid-infrared glass fibres and waveguides as well as optical switches and photonic integrated circuits, GaN-based optoelectronic devices and high power semiconductor lasers. The CAMERA centre houses PIV and ESPI systems and expertise, IBIOS applies state of the art developments in optical imaging technology to research in cellular biology. Other innovative laser based characterisation techniques include laser-generated surface acoustic waves. Our internationally recognised activity in high-power laser diodes, including simulation/design and degradation physics has been supported by 6 EC and 2 industrial grants. www.nottingham.ac.uk

World of Medicine - Erika Mase, Marketing Manager

WOM is a pioneer and world leader in the field of Minimally Invasive Medicine. As a medical device company with an international focus, we have been developing and producing innovative products for over 40 years, that make surgeries in arthroscopy, cardiology, hysteroscopy, laparoscopy, oncology, and urology, as easy as possible on patients. The needs of our customers are always the focus of our efforts - from individual branding to a distinctive product and interface design. All WOM products are characterized by their ease of use and compact modular design. With its four core competencies, WOM offers a broad spectrum of equipment as well as disposable products: Cameras & Photonics, Insufflaters & Pumps, Cardiac-Thoracic Instruments, Disposables.

EPIC workshops promote a strong interaction and facilitate understanding between clinicians-industry-research
Development of Mid IR fiber optics within the last decade enables biomedical applications of FTIR-spectroscopy not only for in-vitro, but for in-vivo diagnostics. While in the past fiber coupled FTIR-spectrometers were produced with LN-cooled MCT detectors, now very good S/N Ratio can be reached with room temperature DTGS-detectors. High quality Polycrystalline PIR-fibers from Silver Halide crystals and Chalcogenide As-S-glass CIR-fibers provide good throughput in optimal coupling with FTIR - making biomedical diagnostics possible using ATR absorption and reflectance spectroscopy in Mid IR - the most informative finger-print region for organic molecular vibrations.

FTIR spectrometers equipped by DTGS-detectors & coupled with ATR-fiber probes by mirror-fiber couplers installed in sample chambers.

ATR-Probes

ATR-Absorption Spectroscopy with detachable PIR-fiber loops enable molecular analysis of liquids and tissue in-vivo, in real-time, including endoscopic applications, in two parts of Mid IR-range (due to use of CIR- or PIR-fibers): 6500-1700cm⁻¹ and 3600-600cm⁻¹.

Fig. 4. Transmission spectra of different ATR-probes of 1.5m length and design of detachable single & multi-loop ATR-tips.

ATR-probes with detachable tips based on PIR-Loops (or other ATR-tips – like Silicon or Diamond-cone) enables to sterilize them and to use for diagnostics in-vivo (which is also needed for disposable PIR-loops).

Fig. 5 Examples of ATR-absorption spectra for a hand skin.

Sterilization is needed for all biomedical applications in-vivo and it was tested for detachable PIR-Loop ATR-tips. Spectral overlay of bovine cartilage after sterilization does not show any significant changes in the Amide I & II peak heights

Fig. 6. Photos of PIR-loops glued in detachable PEEK-caps & Absorption spectra of bovine cartilage after PIR-Loops sterilization

FTIR-spectroscopy with ATR-Fiber Probes in biomedical applications

Pioneering applications of FTIR-fiber spectroscopy were started long time ago to detect malignant tissue during cancer operation (#1) and now much more trials are done in-vivo (#2) & in-vitro (#3) – see data presented from 3 articles at Fig. 7 to show great potential of FTIR-spectroscopy for molecular tissue diagnostics.

Fig. 3. Fabry-Perot Spectral Engine from VTT vs iSS


#2. Spectra of normal Blue), necrotic (green) and carcinoma (red) brain tissue.

N.Bergner et al., Analyst, 2013, 138, 3983