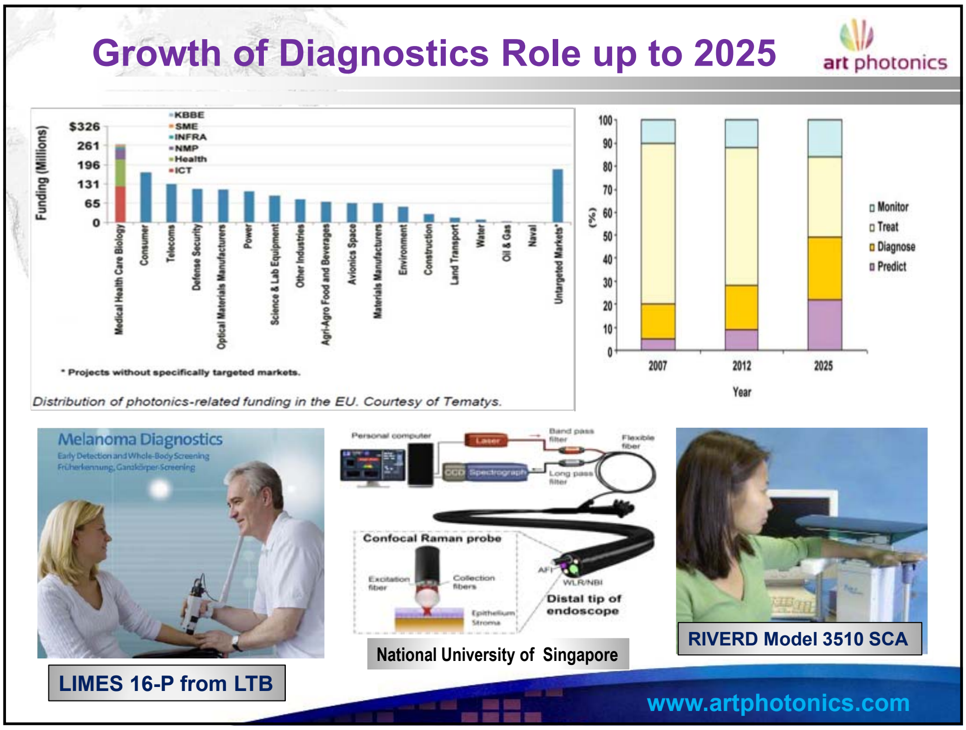
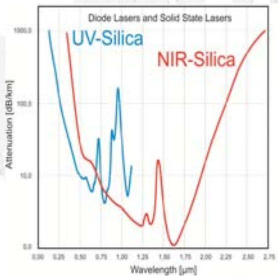
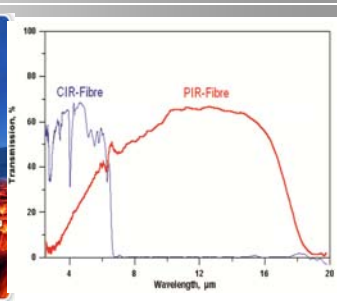

art photonics
СВЕТОВОДНАЯ ФОТОНИКА ДЛЯ БИОМЕДИЦИНЫ
– ОТ ЛАЗЕРНОЙ МЕДИЦИНЫ ДО ДИАГНОСТИКИ
Viacheslav Artyushenko
art photonics GmbH, Berlin
Institute of General Physics, Moscow
CHARITÉ
2-nd School on ADFLIM
St-Petersburg, July 26-28, 2017


Growth of Diagnostics Role up to 2025
art photonics
Funding (Millions)
$326
261
196
131
65
0
KBBE
SME
INFRA
NMP
Health
ICT
Medical Health Care Biology
Consumer
Telecoms
Defense Security
Optical Materials Manufacturers
Power
Science & Lab Equipment
Other Industries
Agri-Agro Food and Beverages
Avionics Space
Materials Manufacturers
Environment
Construction
Land Transport
Water
Oil & Gas
Naval
Untargeted Markets*
* Projects without specifically targeted markets.
Distribution of photonics-related funding in the EU. Courtesy of Tematys.
(%)
Monitor
Treat
Diagnose
Predict
2007
2012
2025
Year
Melanoma Diagnostics
LIMES 16-P from LTB
Personal computer
Laser
CCD Spectrograph
Band pass filter
Long pass filter
Flexible fiber
Confocal Raman probe
Excitation fiber
Collection fibers
Epithelium
Stroma
Distal tip of endoscope
National University of Singapore
RIVERD Model 3510 SCA
www.artphotonics.com

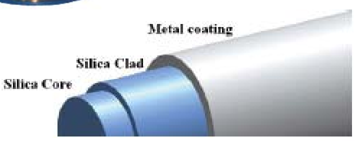
Metal coated Silica and CIR- & PIR-fibres

art photonics

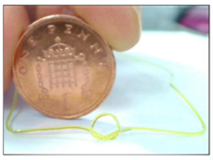


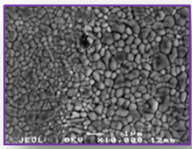


Alu- or Copper coating for Silica fibres to be used up to 350-600°C



Polycrystalline IR-fibres for Mid IR-range: 3-18µm
PIR-fibres are produced by patented technology by *extrusion of Silver Halide solid solution crystals*

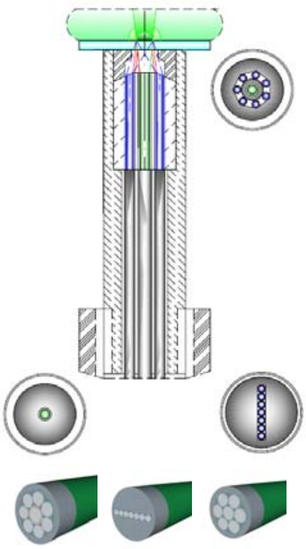


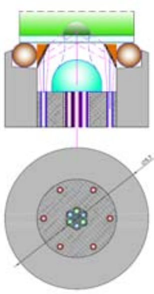


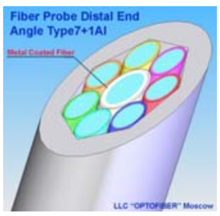
www.artphotonics.com

Fiber Probes for Fluorescence, Raman and Diffused Scattering Spectroscopy

art photonics





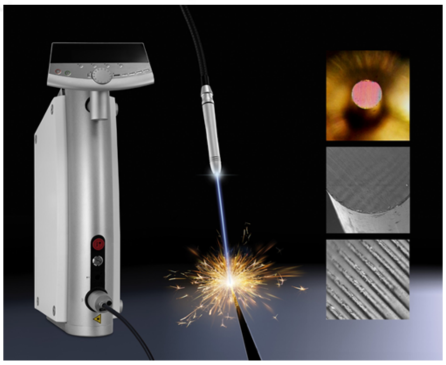


www.artphotonics.com

Mid IR-Fibers Cables for Laser Medicine

art photonics

High Power Cables based on Mid-IR-fibers provide flexible delivery for laser radiation in a broad spectral range. They can be used with various IR-lasers – from solid state Ho- & Er:YAG to HF-, DF-, CO- & CO_2-gas lasers. Special design of HP-connectors enables long life of HP-cables made with IR-fibers, while special SMART-treatment of fiber ends helps to suppress Fresnel reflection during laser power delivery. Absence of AR-treament will lead to too high Fresnel loss above 30% due to a high refraction index of Mid IR-fibers



www.artphotonics.com

IR-fiber coupled CO-Laser & Biotissue

art photonics

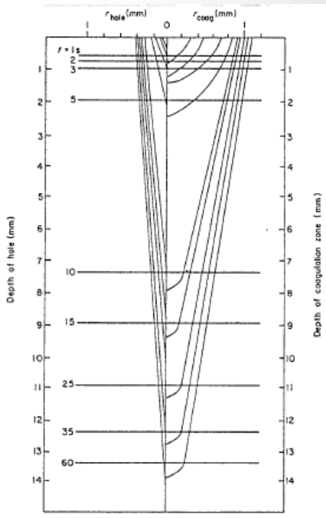


Fig. 2 Cross-section of both the hole and coagulation zone in the muscle tissue when the irradiance on its surface was 2.5 kW cm^{-2} and the irradiation time, t, was 1,2,3,5...60 s. r_{hole} and r_{coag} are the radii of the hole and coagulation zones, and h_{hole} and h_{coag} are the depths of the hole and coagulation zone

Coagulation and destruction of biological tissue by CO laser irradiation using fibre-optic cable

A.O. ABAKUMOV, V.S. ALEINIKOV, V.G. ARTJUSHENKO, V.P. BELYAEV, L.N. BUTVINA, L.K. BOGUSH, V.V. VOJTSEKHOVSKY, N.D. DEVYATKOV, E.M. DIANOV, V.G. DOBKIN, V.I. MASYCHEV, A.M. PROKHOROV, V.K. SYSOEV

The first results on the use of a flexible fibre-optic cable (based on KRS–5 fibre) for the transmission of CO laser power to the operating zone for the coagulation and destruction of biological tissue are presented.

OPTICS AND LASER TECHNOLOGY . AUGUST 1986

The 1st CO-lasers (sealed off, water cooled) were tested in experimental trials with rabbits in 1984-86. Output cw power of 7W was delivered by PIR-fiber cable of 1,2m length and refocused to tissue with output lens

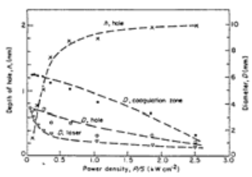
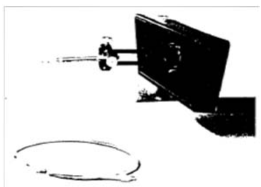
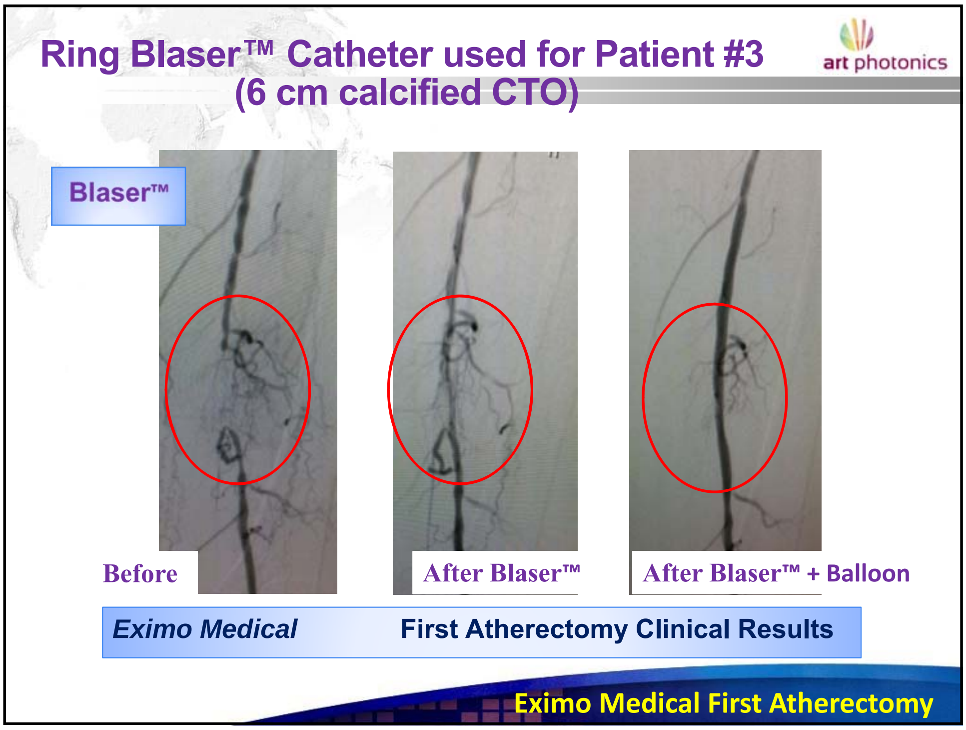


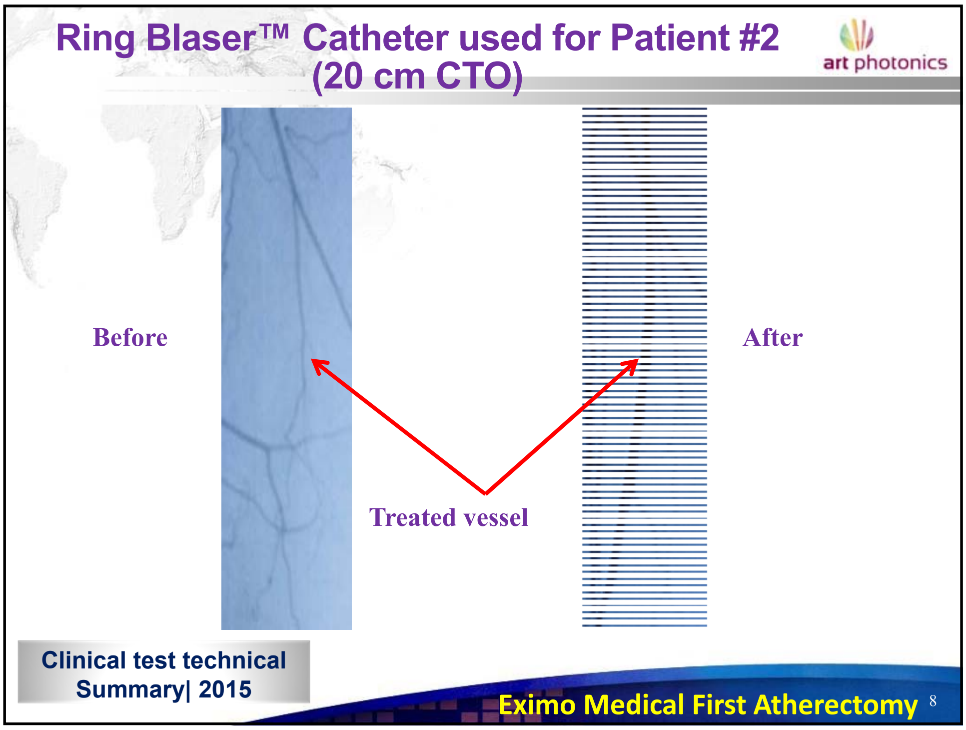
Fig. 1 The dependences of the laser beam diameter (D_{laser}), coagulation diameter (D_{coag}), hole diameter (D_{hole}) and depth of the hole (h_{hole}) in the rabbit muscle tissue in vitro, on the irradiance. The laser radiation power was 7 W, and irradiation time 5 s



ILGN-706 laser radiator with fibre-optic cable

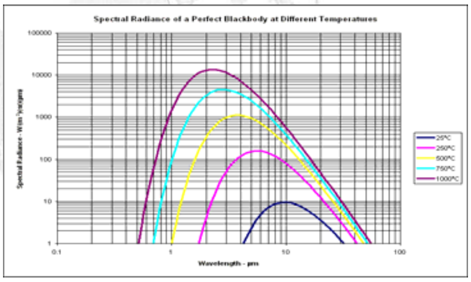
www.artphotonics.com

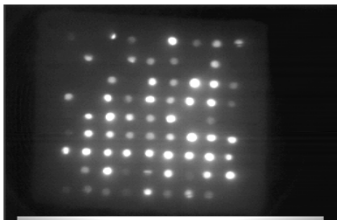

Ring Blaser™ Catheter used for Patient #3
(6 cm calcified CTO)
art photonics
Blaser™
Before
After Blaser™
After Blaser™ + Balloon
Eximo Medical
First Atherectomy Clinical Results
Eximo Medical First Atherectomy


Ring Blaser™ Catheter used for Patient #2
(20 cm CTO)
art photonics
Before
After
Treated vessel
Clinical test technical
Summary| 2015
Eximo Medical First Atherectomy
8

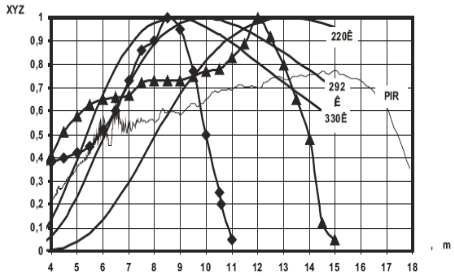
Mid IR-Fiber Pyrometry

art photonics





9x9 PIR-fiber coherent bundle



www.artphotonics.com

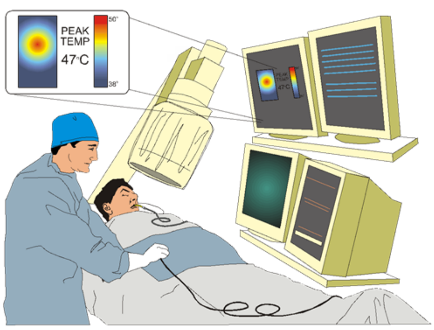
SECURUS MEDICAL GROUP

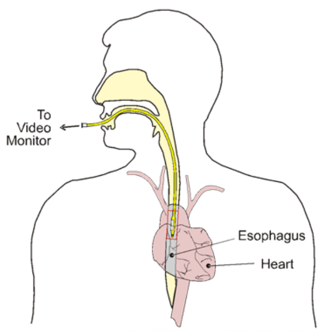
art photonics

Thermographic Imaging System

Monitor: Continuous, high-resolution thermal image

Probe: Esophageal infrared thermal mapping catheter

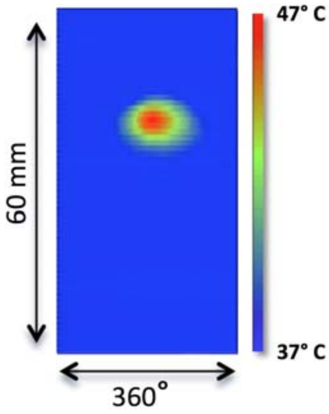


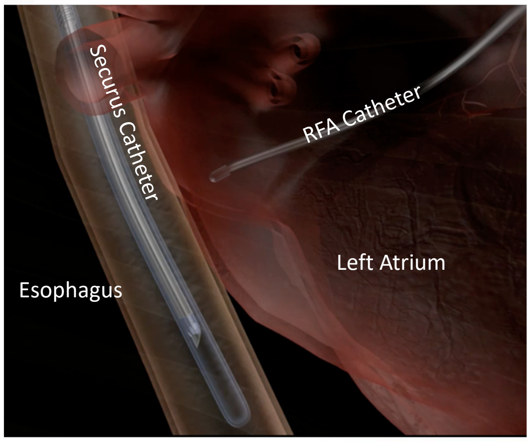


www.artphotonics.com

SECURUS MEDICAL GROUP

Securus System





www.artphotonics.com

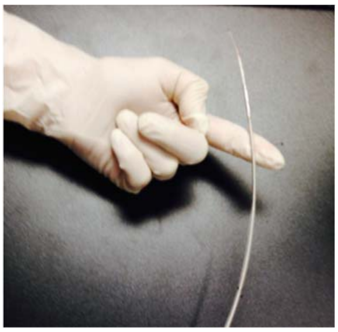
SECURUS MEDICAL GROUP

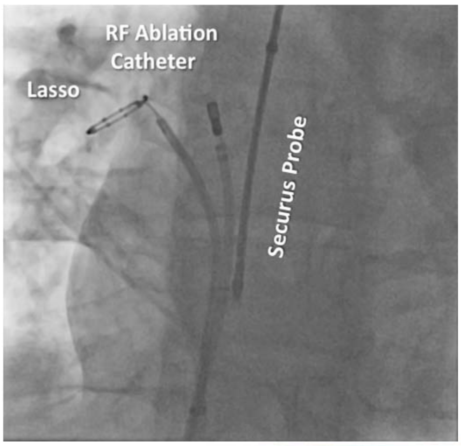
Securus Infrared Probe

Flexible, 9 Fr (3 mm)

Oral or Nasal Insertion

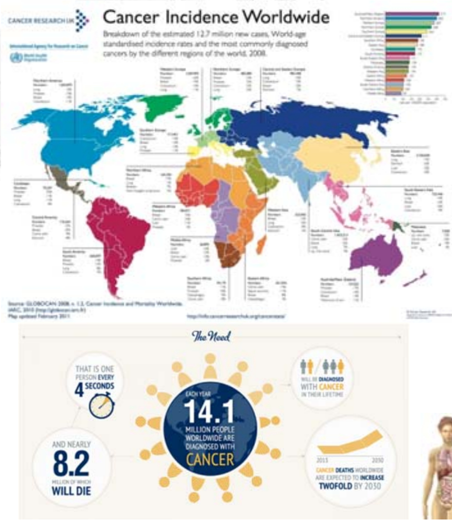
Radio-opaque



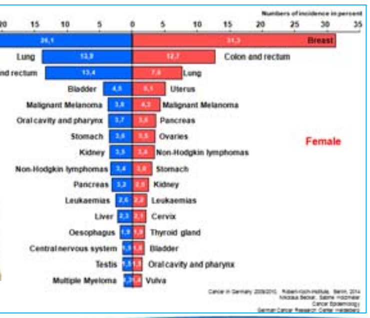


Tumor patients in Germany and worldwide

art photonics



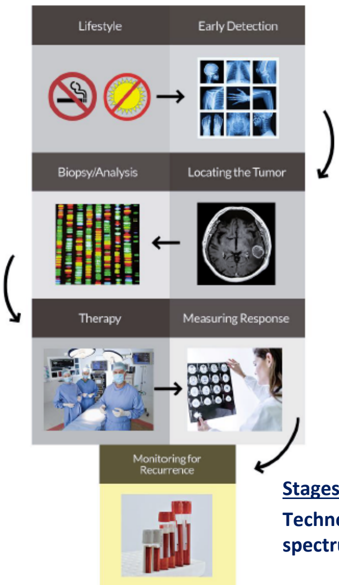
Cancer hang over the soul like a black cloud



www.artphotonics.com

NPI: CANCER MOONSHOT TASK FORCE

art photonics



A BRIGHTER FUTURE: ELIMINATING CANCER THROUGH ADOPTION OF NEW AND ENHANCED TECHNOLOGIES AND A TRANSFORMED IT HEALTH SYSTEM

JUNE 29, 2016

NPI road map is made jointly by the scientific community, medical technology industry, more than 350 hospitals, and major patient advocacy groups - to apply more than $3 billion yearly in private investments to technology for early detection of the most aggressive cancers.

NATIONAL PHOTONICS INITIATIVE

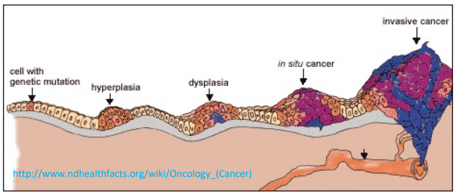
Stages of cancer detection and treatment

Technologies impact patients across the cancer treatment spectrum, from prevention and early detection to treatment.

www.artphotonics.com

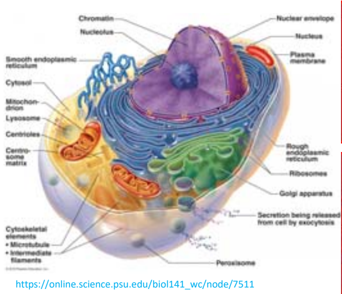
Spectroscopic methods for tumor diagnosis

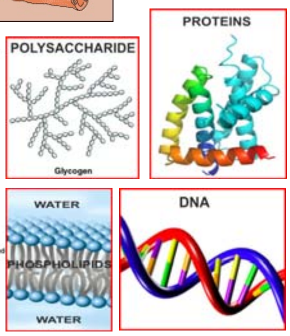
Deciphering the molecular fingerprints of diseases stays high on the priority list of biomedical research. Detailed knowledge in chemical composition changes in pathological cell and tissue functions will affect the development of novel diagnostic and therapeutic approaches.

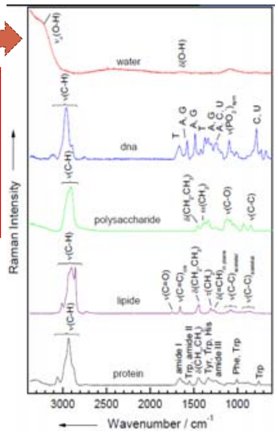


A vibration spectrum reflects the condition of all cell components in the tissue at the point measured. Each spectrum is like a "fingerprint" for the change, unique and characteristic.

Cell components:

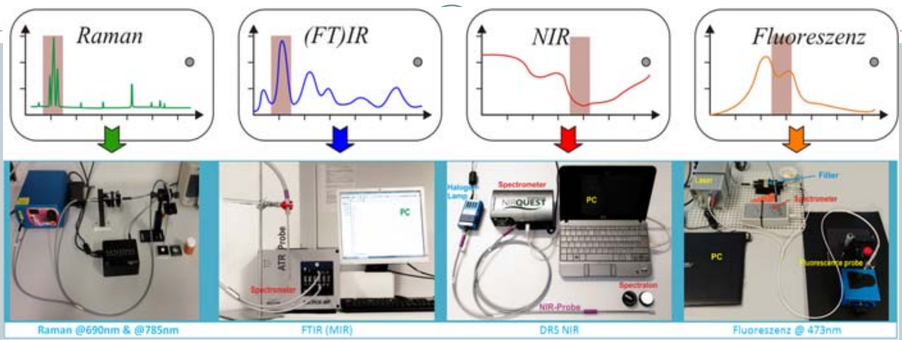






www.artphotonics.com

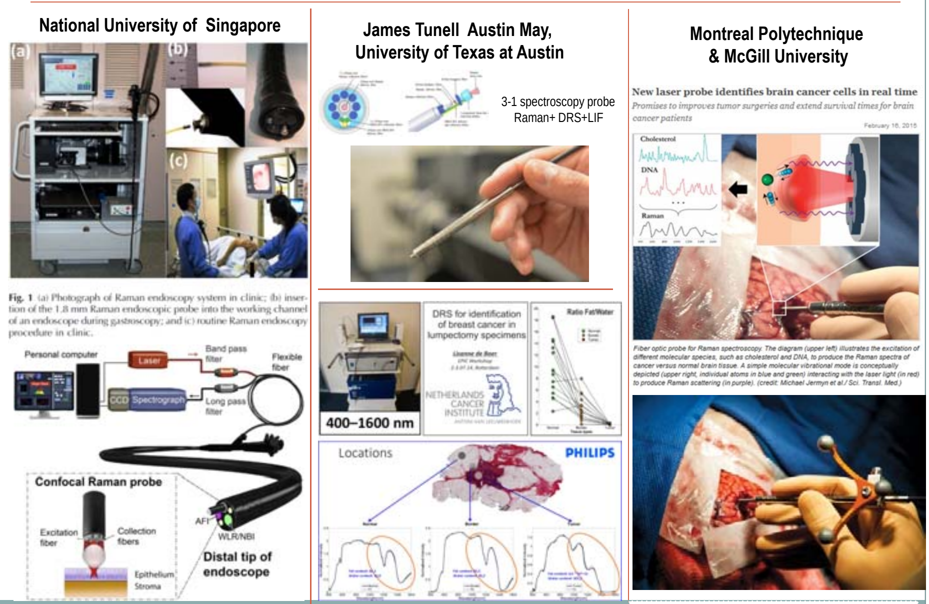
Label Free Fiber Spectroscopy Methods



Spectroscopy methods should be compared to select the best one or their best combination to find the most sensitive, specific and accurate for cancer detection. Correct comparison of all methods must be done for the same spot of tissue in a short time. An additional demands for any spectral diagnostics system are evident: portability, low cost and friendly software.

www.artphotonics.com

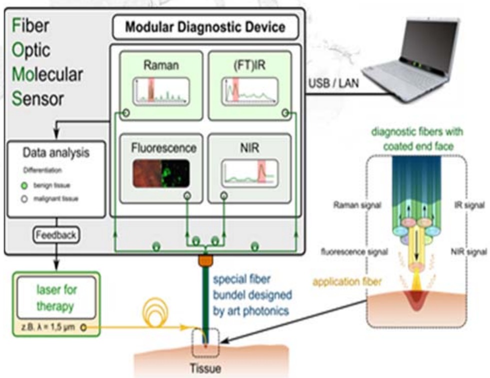
3 Spectroscopy Methods Coming to Clinics



www.artphotonics.com

Fiber Spectroscopy for Cancer Detection

art photonics



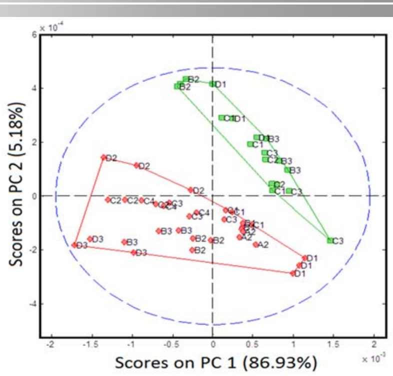


Fig.7 PCA analysis of kidney tissue based on MIR spectra

Spectroscopy method or their optimal combination should be compared and selected to find the best sensitivity, specificity and accuracy in definition of tumor margins. Correct comparison of all methods must be done with the same tissue sample in a short time. Evident demands on spectral systems for clinical diagnostics are also: portability, low cost and friendly software.

www.artphotonics.com

Medical Demands on Tiny Fiber Probes

art photonics

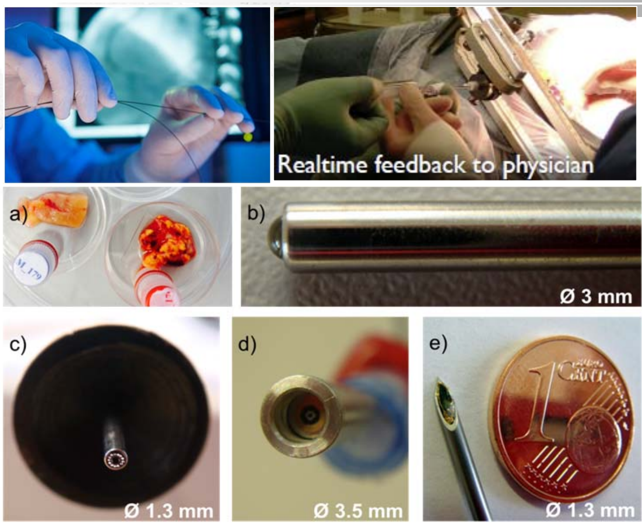


Fig.2 a) renal samples, b) Raman probe with ball lens, c) fluorescence probe, d) NIR probe, e) MIR needle

Demands to Medical Fiber Probes:

- small diameter
- highly flexible
- biocompatible
- sterilizable or
- disposable
- easy detachable
- compatible with endoscopes or catheters
- of stable & high transmission under bending
- of low cost

www.artphotonics.com

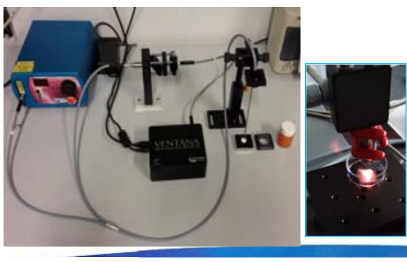
Label Free Fiber Spectroscopy Methods

NIR-DRS-set from Ocean Optics

Fluorescence equipment

FT-IR from Bruker (Matrix-MF)

Raman-spectrometer (Ocean Optics)



www.artphotonics.com

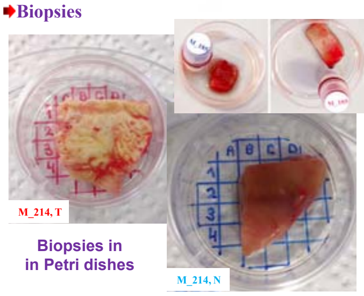
Biopsy Samples: *in-vitro (10) & ex-vivo (1)*

Renal cell carcinomas (RCC)

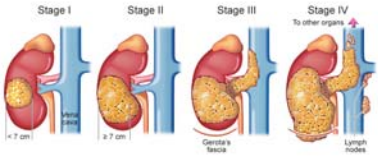
Left kidney, clear cell renal carcinoma, pT1aG2R0L0V0, after Perfusion

Clear cell renal carcinoma, pT3bG3R0L0V2 with Cava Thrombus), without Perfusion

Biopsies



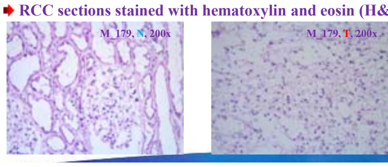
Stages of RCC



Nr.	Gender	Age	Histol. Typ	Morphology	Staging pT	Grad
M_178	f	37	3	8317/3	2b	2
M_179	f	73	1	8310/3	3a	2
M_185	f	58	1	8033/3	3a	3
M_191	f	66	1	8310/3	1a	2
M_194	m	57	1	8310/3	3b	2
M_198	m	59	1	8310/3	3a	3
M_144	m	62	1	8310/3	3a	2
M_149	m	56	1	8310/3	1b	1
M_151	m	69	1	8310/3	3a	2
M_160	m	47	1	8310/3	2b	2
M_214	m	38	1	8310/3	3a	3

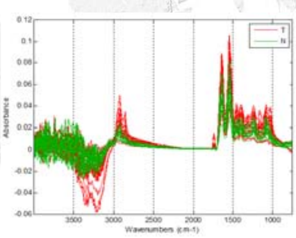
1—Clear Cell RC, 3-Chromophobe RC

RCC sections stained with hematoxylin and eosin (H&E)

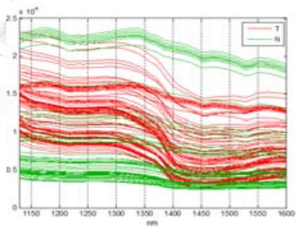


Spectra Measured for Kidney Biopsies

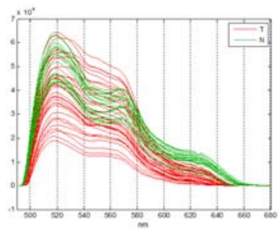
FT-IR-Spectra



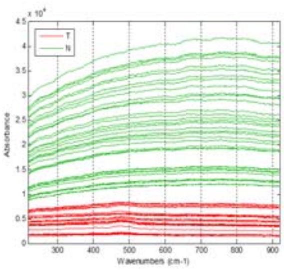
NIR Spectra (1129-1600 nm)

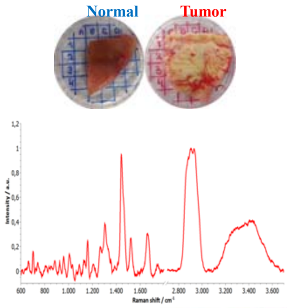


Fluorescence (Excitation 475nm)

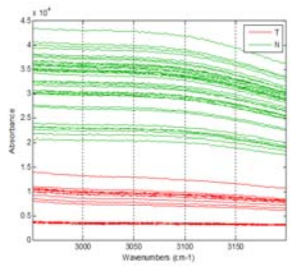


Raman - Excitation 785nm



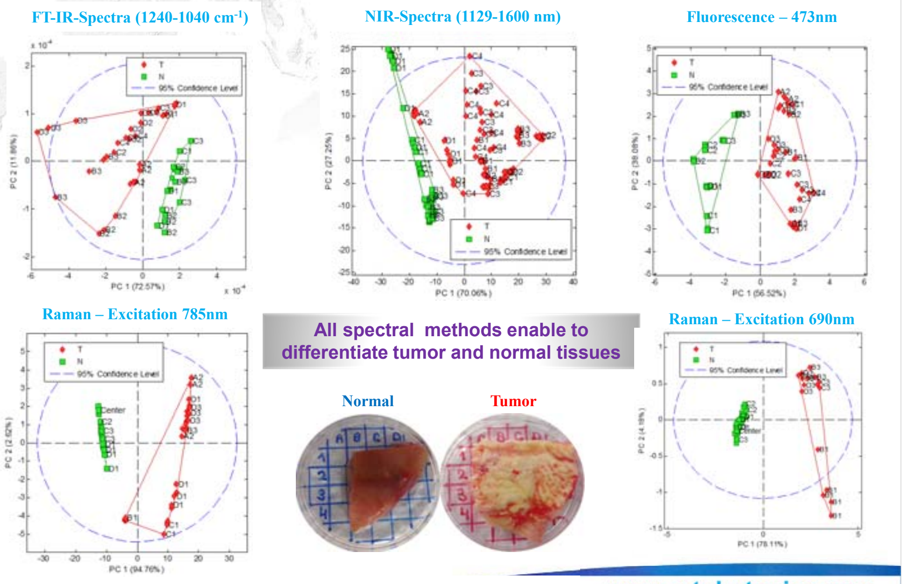


Raman - Excitation 690nm



www.artphotonics.com

Chemometric Analysis for Spectra of Biopsies

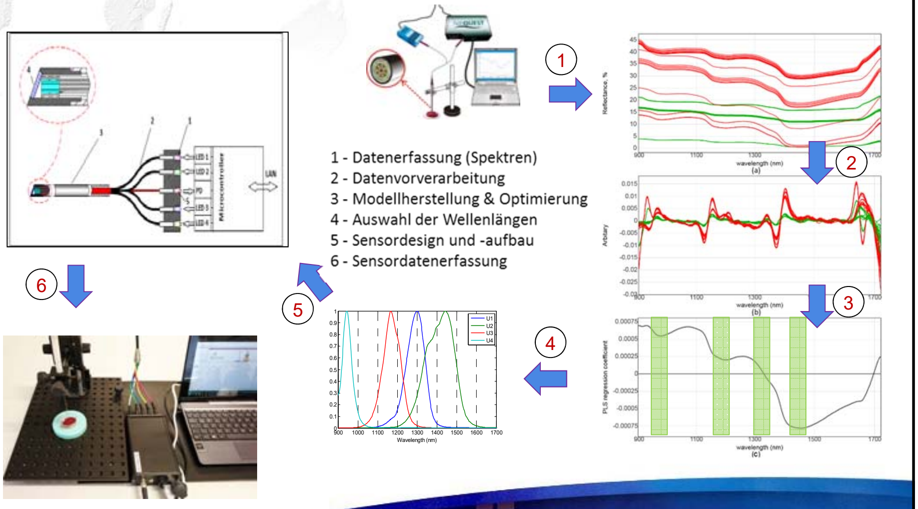


www.artphotonics.com

AP-4.3 Transfer auf die Sensor-Ebene (FOMoS)

art photonics

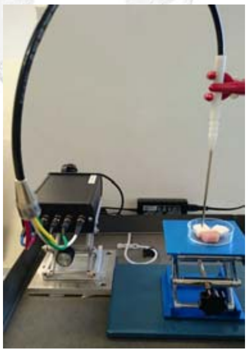
- Die Modelle, die auf den Spektrometermessungen basieren, müssen nun durch entsprechende Maßnahmen an die Sensoren angepasst werden



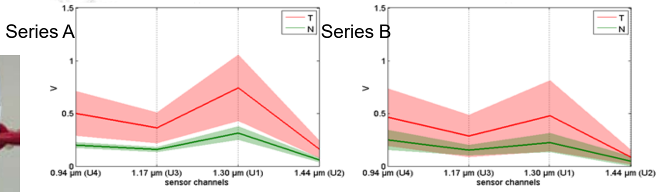
1 - Datenerfassung (Spektren)
2 - Datenvorverarbeitung
3 - Modellherstellung & Optimierung
4 - Auswahl der Wellenlängen
5 - Sensordesign und -aufbau
6 - Sensordatenerfassung

AP-4.3 Transfer auf die Sensor-Ebene (FOMoS) (2)

art photonics



LED-Sensordaten: Mittelwert und Standardabweichung



Data	Calibration								Cross-validation							
	DQ^2	TP	FP	TN	FN	%Sn	%Sp	%Ac	DQ^2	TP	FP	TN	FN	%Sn	%Sp	%Ac
An41[a]	0.932	21	0	20	0	100	100	100	0.920	21	0	20	0	100	100	100
As41[b]	0.917	21	0	20	0	100	100	100	0.488	21	0	20	0	100	100	100
As33[c]	0.413	19	1	11	2	91	92	91	0.358	18	1	11	3	86	92	88
Bs170[d]	0.181	62	5	70	33	65	93	78	0.153	59	7	68	36	64	92	75
Bs140[e]	0.500	64	3	67	6	91	96	94	0.478	63	3	67	7	90	96	93

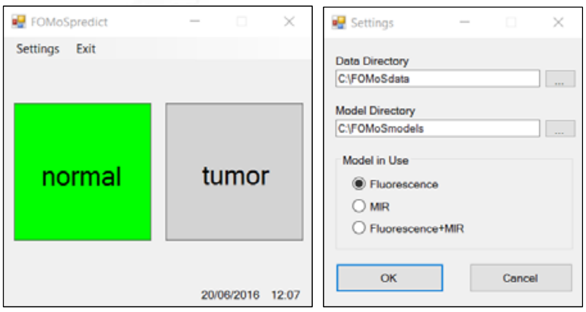
Die Sensordaten erlauben die Klassen T/N komplett (Series A) oder teileweise (Series B) zu trennen.

AP-3.1 Aufbau der Diagnoseeinheit

art photonics

- Entwicklung der Software in Abstimmung mit TU Berlin

Diagnostische Software: Diagnosefenster (links) und Einstellungsfenster (rechts)



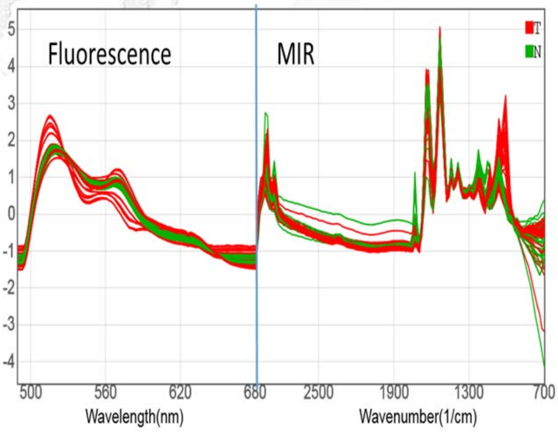
Die Software überwacht kontinuierlich neue Dateien, die von verschiedenen Spektrometern gespeichert werden, liest sie unmittelbar ein und generiert aus den analysierten Daten die Vorhersage.

AP-3.1 Aufbau der Diagnoseeinheit

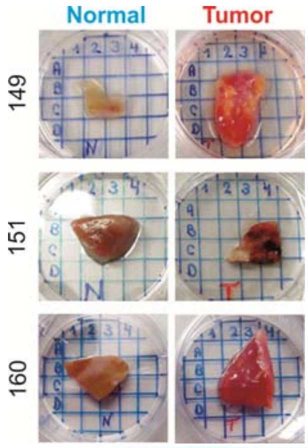
art photonics

- Zuordnung der mathematischen Modelle zur Sondenkonfiguration (1)

Augmentierte Daten Fluoreszenz@473 und MIR-Spektroskopie



3 Patienten, 6 Proben, 79 Messungen

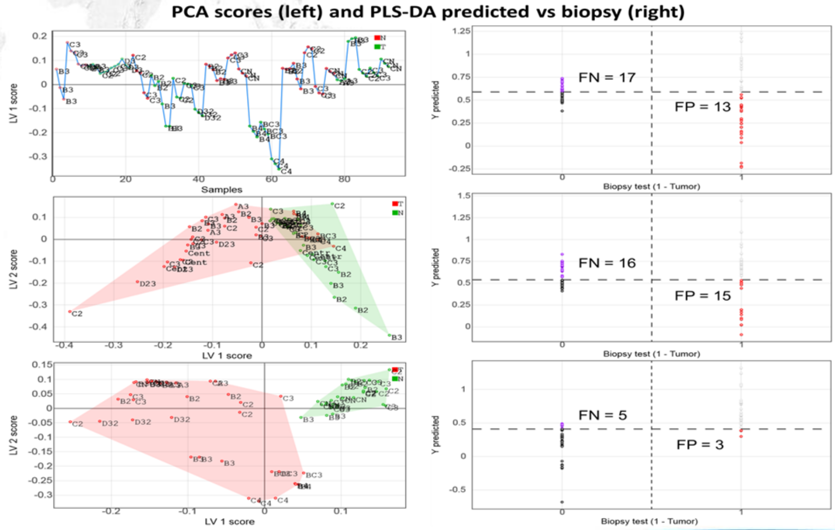


AP-3.1 Aufbau der Diagnoseeinheit

art photonics

Zuordnung der mathematischen Modelle zur Sondenkonfiguration (2)

Data modelling of fluorescence (top), MIR (middle) and their combination (bottom): PCA scores (left) and PLS-DA predicted vs biopsy (right)

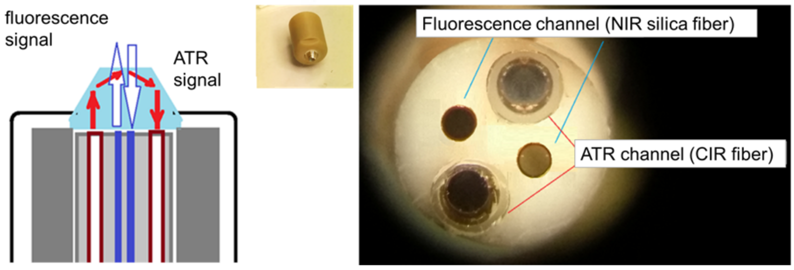


AP-3.1 Aufbau der Diagnoseeinheit

art photonics

- Zuordnung der mathematischen Modelle zur Sondenkonfiguration (3)

Combined ATR-MIR and fluorescence probe: optical scheme (links), ZrO_2 ATR head (middle) and fiber bundle front surface photo (right)



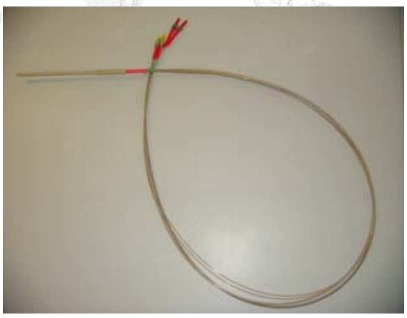
Um die an der gleichen Stelle des Gewebes gemessenen Spektren zu erfassen, wurde eine Kombi-Sonde für die kombinierte ATR-Fluoreszenzmessung entwickelt und hergestellt. Das kompakte Design der Sonde basiert auf der Sonde # 280 mit CIR Fasern und ZrO2 Spitze.

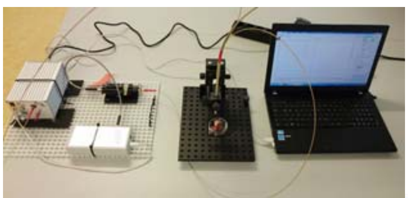
AP-3.1 Aufbau der Diagnoseeinheit

art photonics

- Zuordnung der mathematischen Modelle zur Sondenkonfiguration (4)

ATR-IR + Fluoreszenz Sonde





Für die Anregung und Detektion des Fluoreszenzsignals wurden in die Sonde zusätzliche Quarzfasern eingefügt. Der ZrO2 Kristall hat eine flache Spitze und kann als Fenster für dieses Signal dienen.

Experimental Investigations and quantitative assessments: art photonics GmbH + Charité

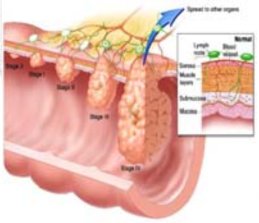
Organ	Amount of Patients (normal+tumor)	Fluore-scence	FT-IR	DRS NIR	Raman @690nm	Raman @785	Assessment of the method * Chemometrical analysis
Kidney	16	++	+++	+	+++	++++	
Stomach	9	++	+	+++	+++	+++	Visual inspection of PLS-DA prediction and score plots from preliminary evaluation on single samples
Peritoneum Omentum	8	+	+	+++	++++	++++	
Colon	6	+++	+++	++	+++	++	
Appendix	3	+++	+	+++	++++	++++	
Rectum	2	+++	----	+	-----	------	
Liver	1	++	+	+++	+++	++++	
Ovary	1	+++	++	+++	++	+	
Lung	1	++++	+++	+	+	++	
PLASMA/SERUM/URINE	N			…			

++++ - very good
+++ - good
++ - moderate
+ - poor , ----- no evaluation

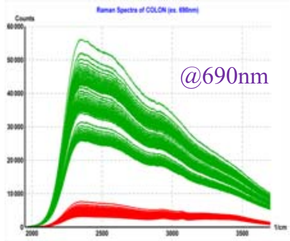
Ongoing sample collection, spectroscopic investigation and data analysis

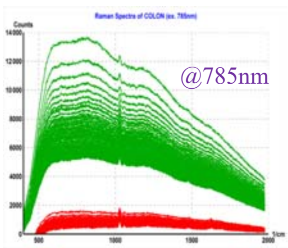
Experimental Investigation. Example of ex vivo measurements on fresh tissue

Colon:

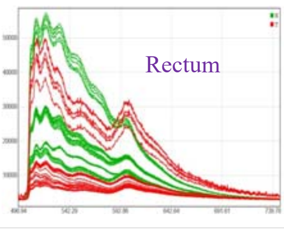


Raman





Fluorescence@473nm



Distal margin of 2 cm from the lower border of colon cancer is sufficient to maintain both intramural and retrograde lymphatics. Guidelines recommend negative margins (> 1 mm) for all rectal cancer patients undergoing resection. The precise definition and control in the identification of the safe time zone is of great importance, since the larger peripheral requirements can lead to nervous disorders and complications in the urinary tract.


art photonics
46
Alexander Prokhorov, 1916
1st SPIE Conference in USSR
„Lasers & Medicine“, 1989
art photonics GmbH
- launched in Berlin in 1998
to develop and produce
specialty fiber products for
applications from 0,2 to 16µm