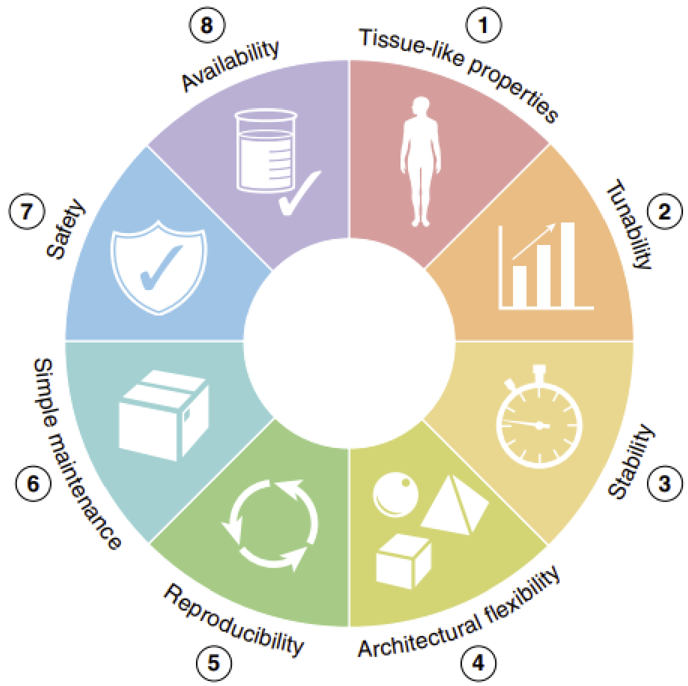
Optical Tissue Phantoms



Brian W. Pogue PhD

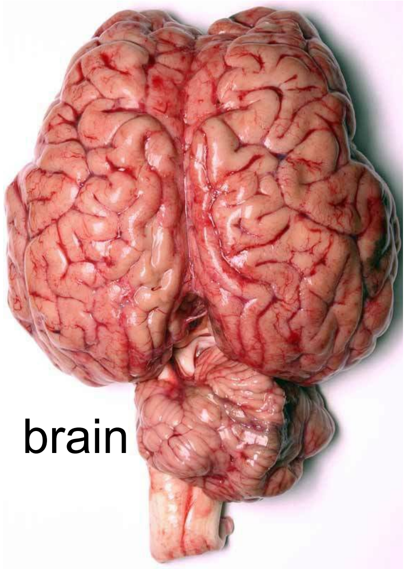
Chair, Department of Medical Physics, University of Wisconsin-Madison

History of Optical Tissue Phantoms

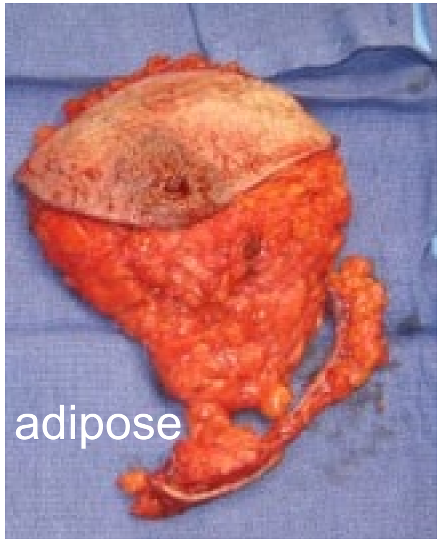
(c1980s)

These are all moderately scattering media

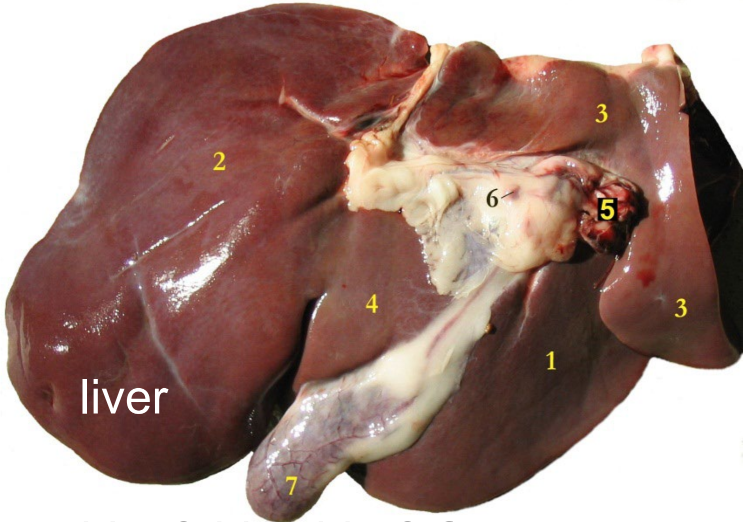
Large variations in tissue optical properties



blood & myelin



fat



bile & bilirubin & fat

methemoglobin

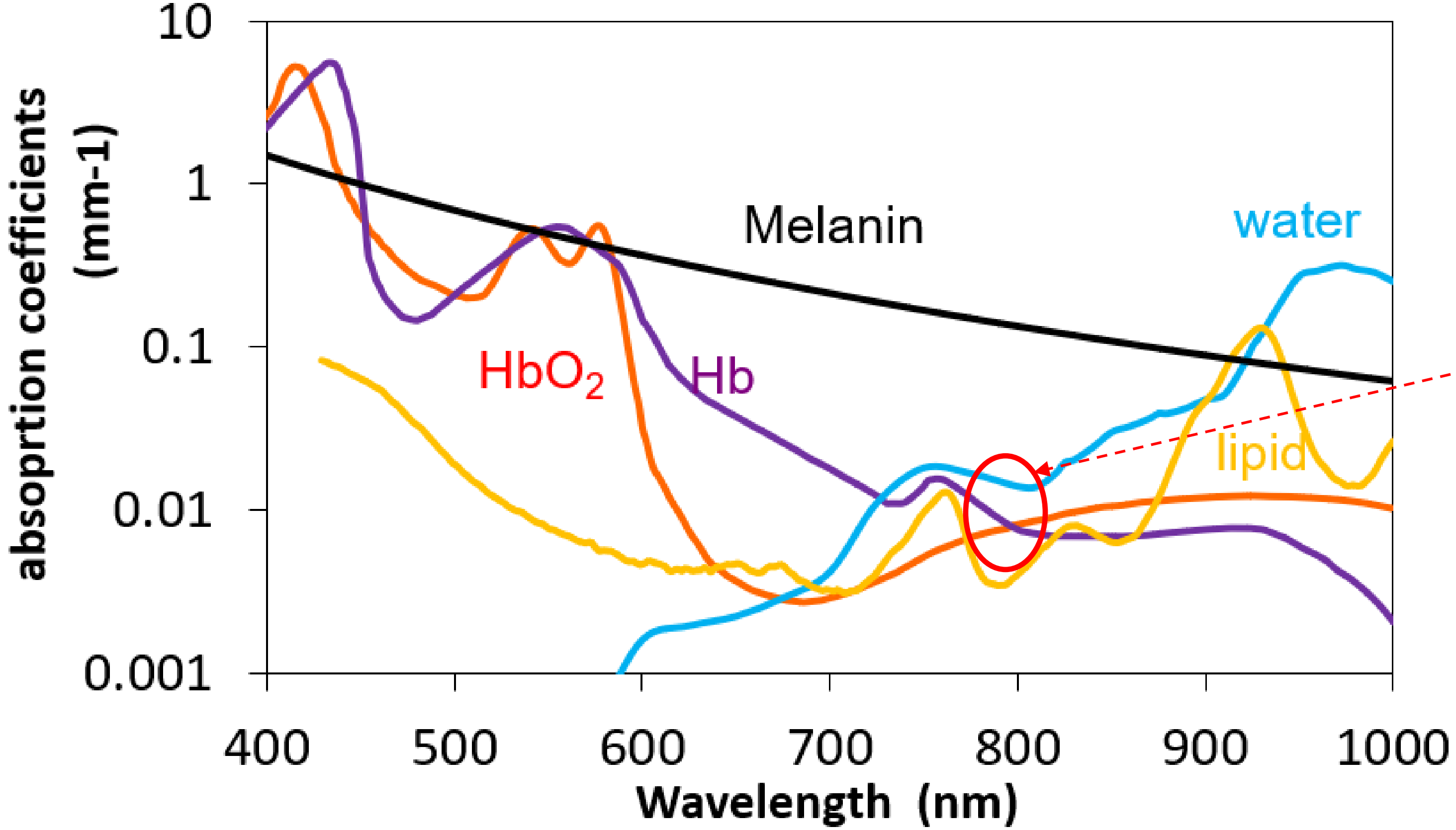
skin

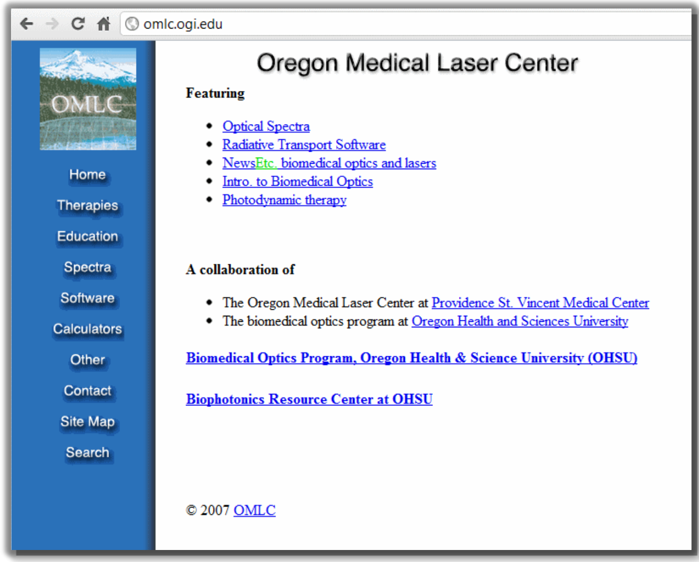
high scatter & melanin

bones

Collagen & minerals

Tissue Absorption Coefficient





$\mu_a \approx 0.01\ mm^{-1}$ at 800 nm

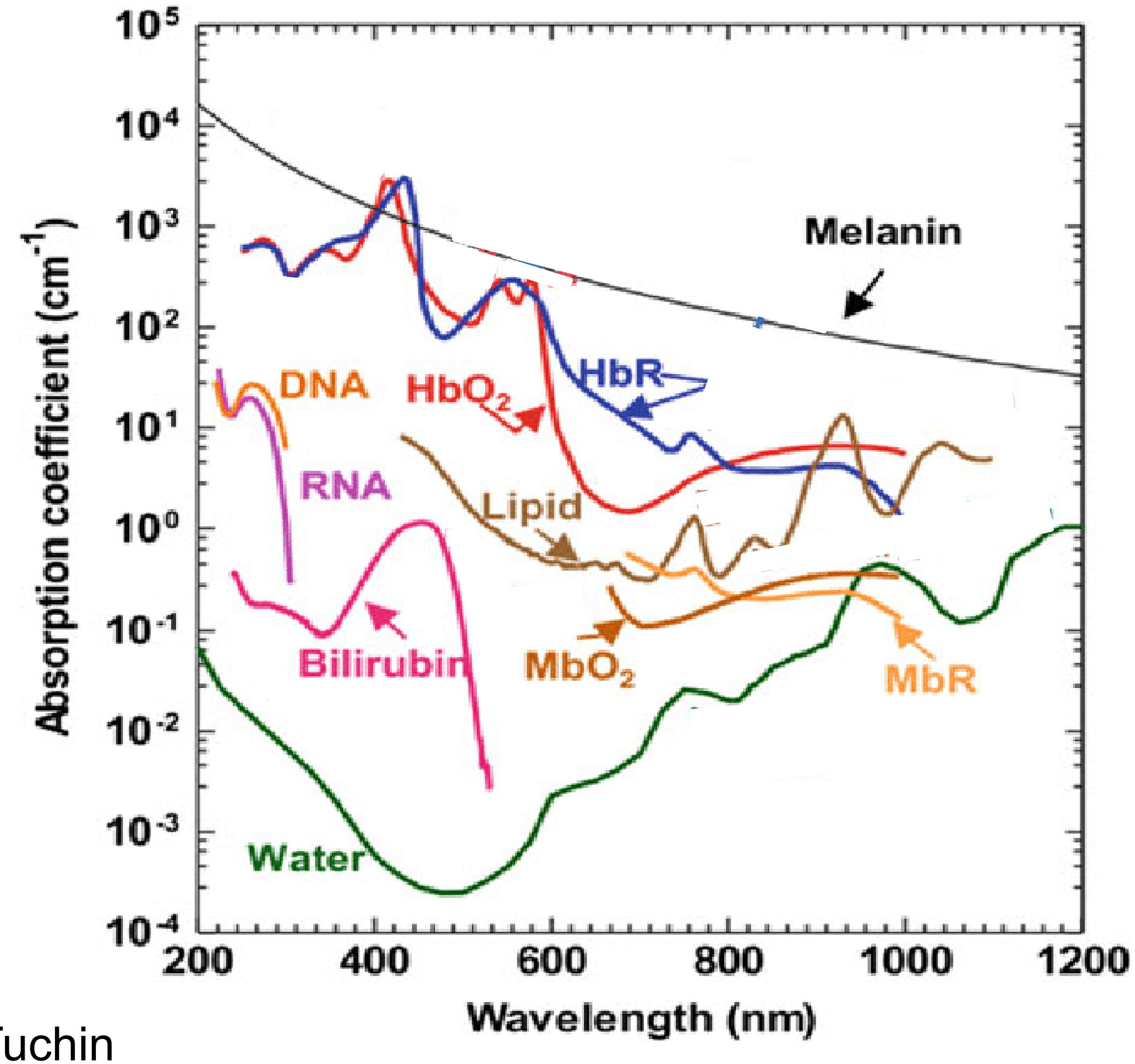
Absorption Coefficient

$$\mu_a = c * e$$

Units: μ_a=[mm^{-1}], c=[μM], e=[$mm^{-1}\ \mu M^{-1}$]

(beware these are typically base e, not based 10 log units)

Tissue Absorption spectrum – a few contributors

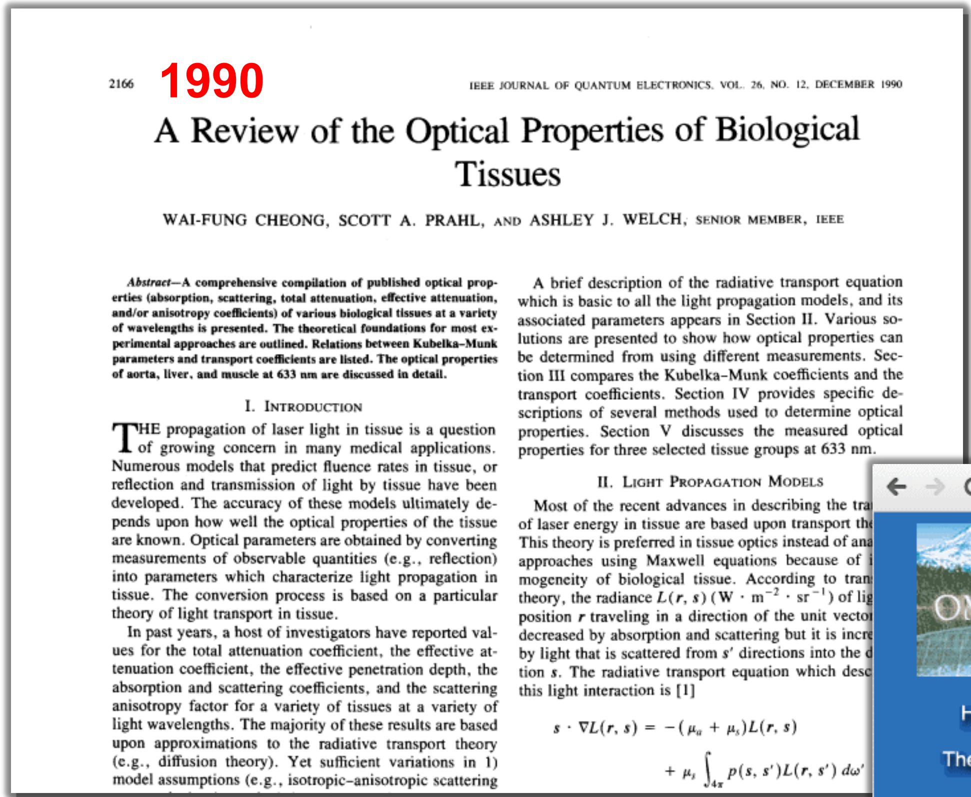


V. Tuchin

Other smaller contributors:
Bilirubin
Methemoglobin
Proteins

Bruise – dynamic Interaction of scattering with hemoglobin & bilirubin

1990


2166 IEEE JOURNAL OF QUANTUM ELECTRONICS, VOL. 26, NO. 12, DECEMBER 1990

A Review of the Optical Properties of Biological Tissues

WAI-FUNG CHEONG, SCOTT A. PRAHL, AND ASHLEY J. WELCH, SENIOR MEMBER, IEEE

Abstract—A comprehensive compilation of published optical properties (absorption, scattering, total attenuation, effective attenuation, and/or anisotropy coefficients) of various biological tissues at a variety of wavelengths is presented. The theoretical foundations for most experimental approaches are outlined. Relations between Kubelka–Munk parameters and transport coefficients are listed. The optical properties of aorta, liver, and muscle at 633 nm are discussed in detail.

I. INTRODUCTION

THE propagation of laser light in tissue is a question of growing concern in many medical applications. Numerous models that predict fluence rates in tissue, or reflection and transmission of light by tissue have been developed. The accuracy of these models ultimately depends upon how well the optical properties of the tissue are known. Optical parameters are obtained by converting measurements of observable quantities (e.g., reflection) into parameters which characterize light propagation in tissue. The conversion process is based on a particular theory of light transport in tissue.

In past years, a host of investigators have reported values for the total attenuation coefficient, the effective attenuation coefficient, the effective penetration depth, the absorption and scattering coefficients, and the scattering anisotropy factor for a variety of tissues at a variety of light wavelengths. The majority of these results are based upon approximations to the radiative transport theory (e.g., diffusion theory). Yet sufficient variations in 1) model assumptions (e.g., isotropic–anisotropic scattering

A brief description of the radiative transport equation which is basic to all the light propagation models, and its associated parameters appears in Section II. Various solutions are presented to show how optical properties can be determined from using different measurements. Section III compares the Kubelka–Munk coefficients and the transport coefficients. Section IV provides specific descriptions of several methods used to determine optical properties. Section V discusses the measured optical properties for three selected tissue groups at 633 nm.

II. LIGHT PROPAGATION MODELS

Most of the recent advances in describing the tra[...] of laser energy in tissue are based upon transport th[...] This theory is preferred in tissue optics instead of ana[...] approaches using Maxwell equations because of i[...] mogeneity of biological tissue. According to tran[...] theory, the radiance $L(r, s)$ $(W \cdot m^{-2} \cdot sr^{-1})$ of lig[...] position r traveling in a direction of the unit vecto[...] decreased by absorption and scattering but it is incr[...] by light that is scattered from s' directions into the d[...] tion s. The radiative transport equation which desc[...] this light interaction is [1]

$$s \cdot \nabla L(r, s) = -(\mu_a + \mu_s)L(r, s)$$

$$+ \mu_s \int_{4\pi} p(s, s')L(r, s')\, d\omega'$$

Cited 3,800 times!!!


AJ Welch

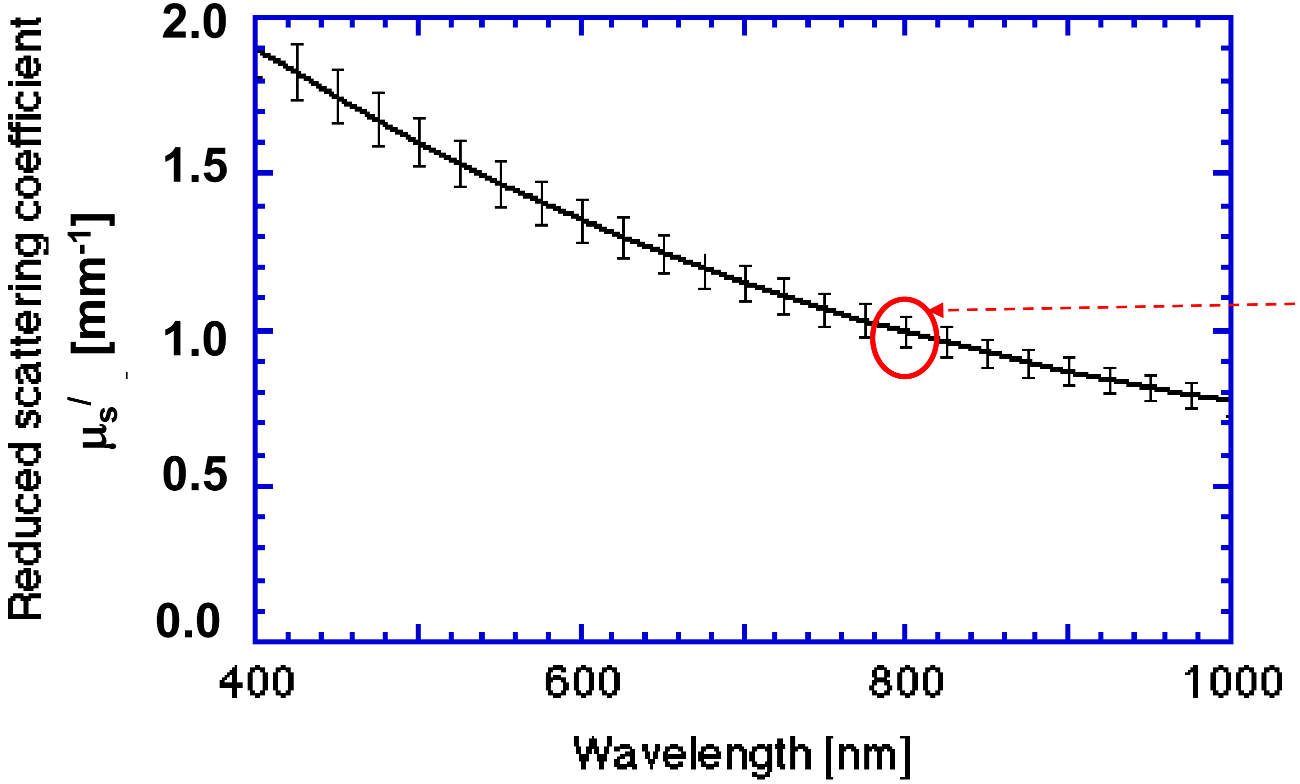

S Prahl


S Jacques

Tissue Scattering spectrum

$$\mu_s^{/}(\lambda) = A\,\lambda^{-b}$$

A – amplitude
b – scattering power
b = 0.9 - 1.4

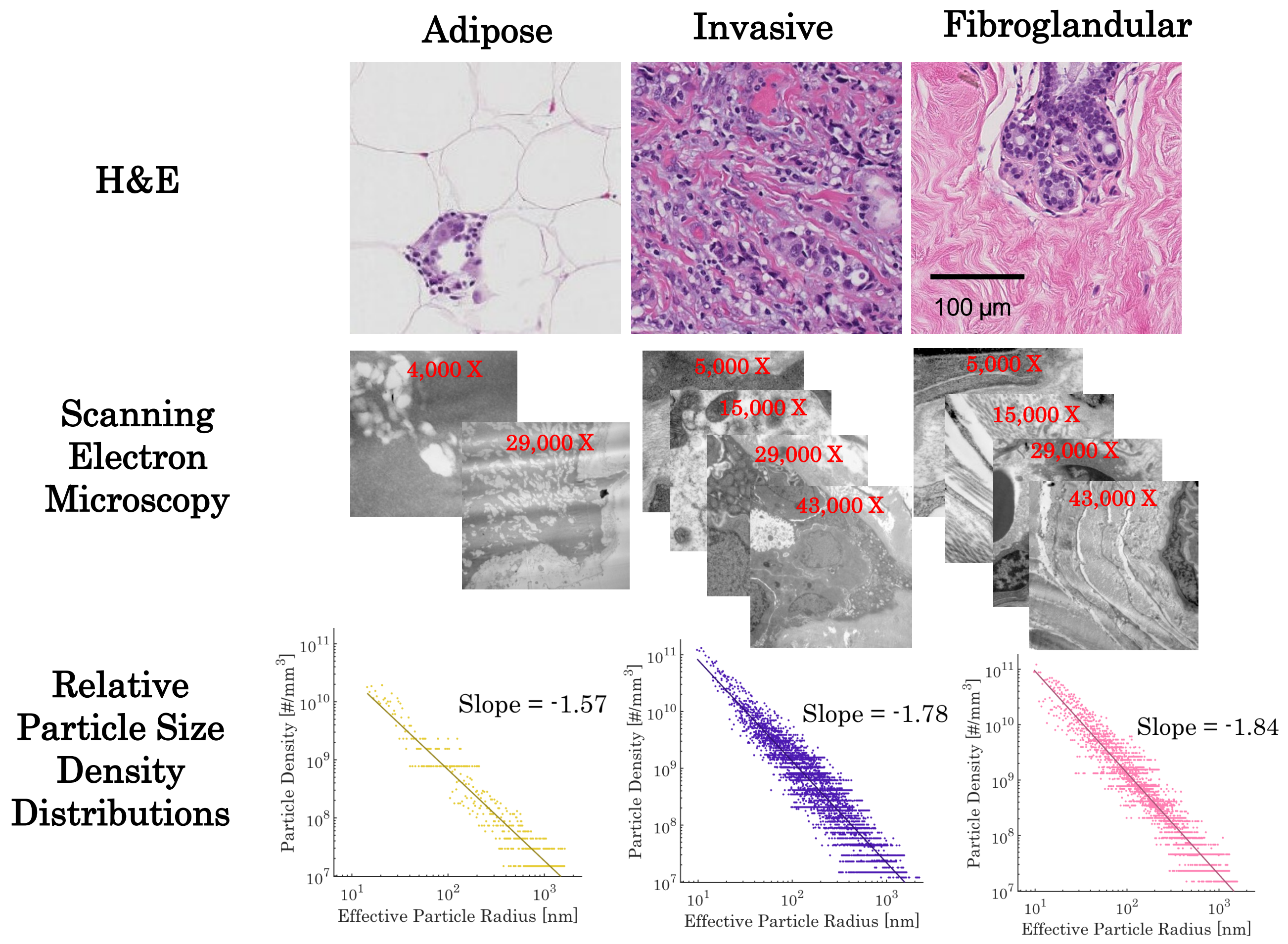


$\mu_s^{/} \approx 1.0$ mm^{-1} at 800 nm

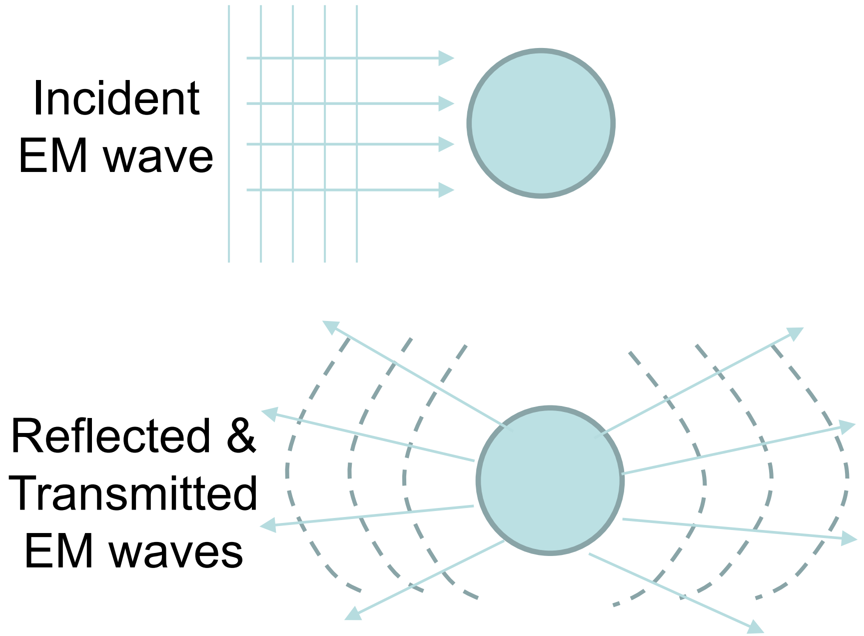
$\mu_a = 0.01$ mm^{-1}, $\mu_s^{/} = 1.0$ mm^{-1}

$\mu_{eff} = 0.17$ mm^{-1}

Tissue is very close to Mie + Rayleigh scatter



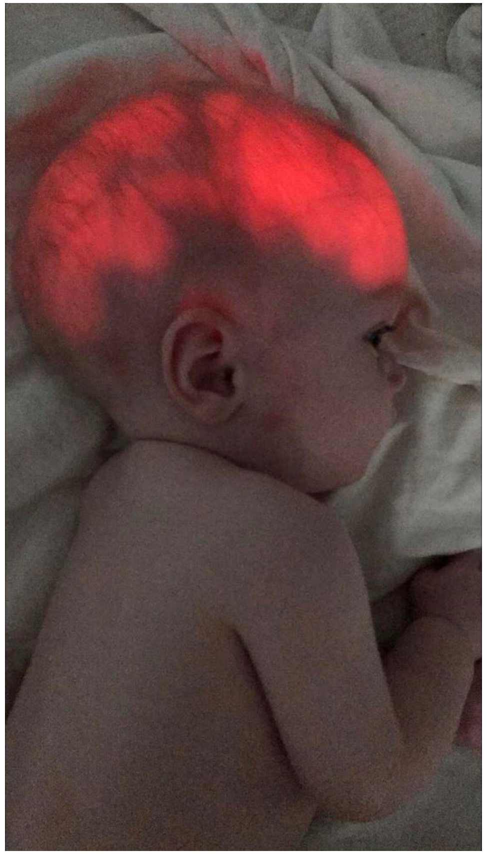
Mie scattering theory:
Plane EM waves scattering from dielectric spheres



Mie theory predicts scatter spectrum

M Bartek, Journal Biomed Optics, 2006

Combination of high scatter & absorption makes tissue translucent

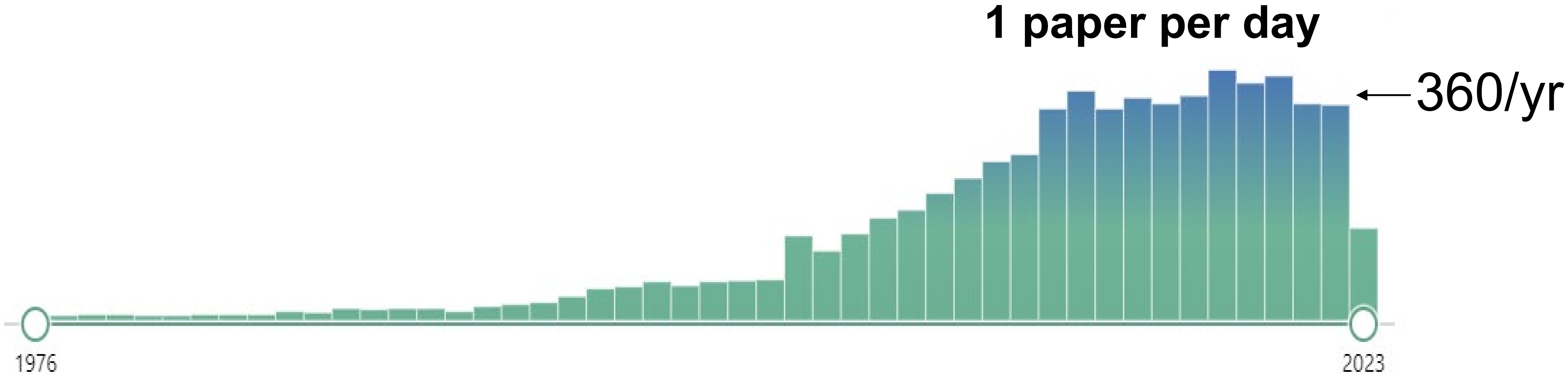


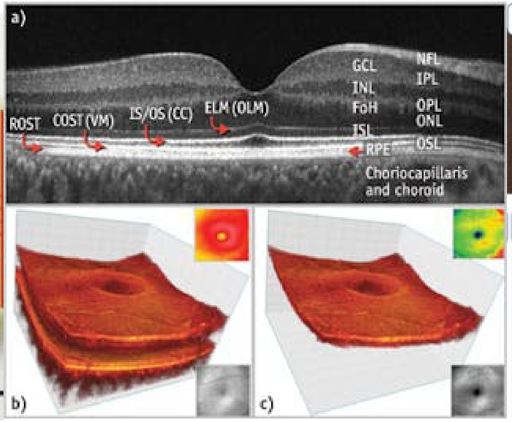
CPR body phantom

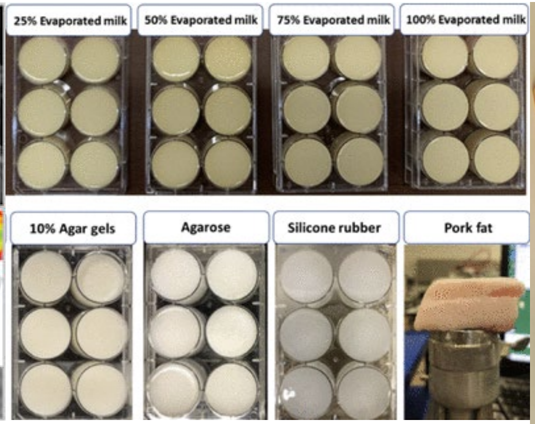
Not translucent

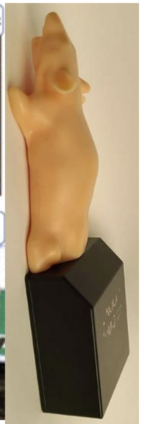
Just the right balance of scatter & absorption

Optical tissue phantom publications



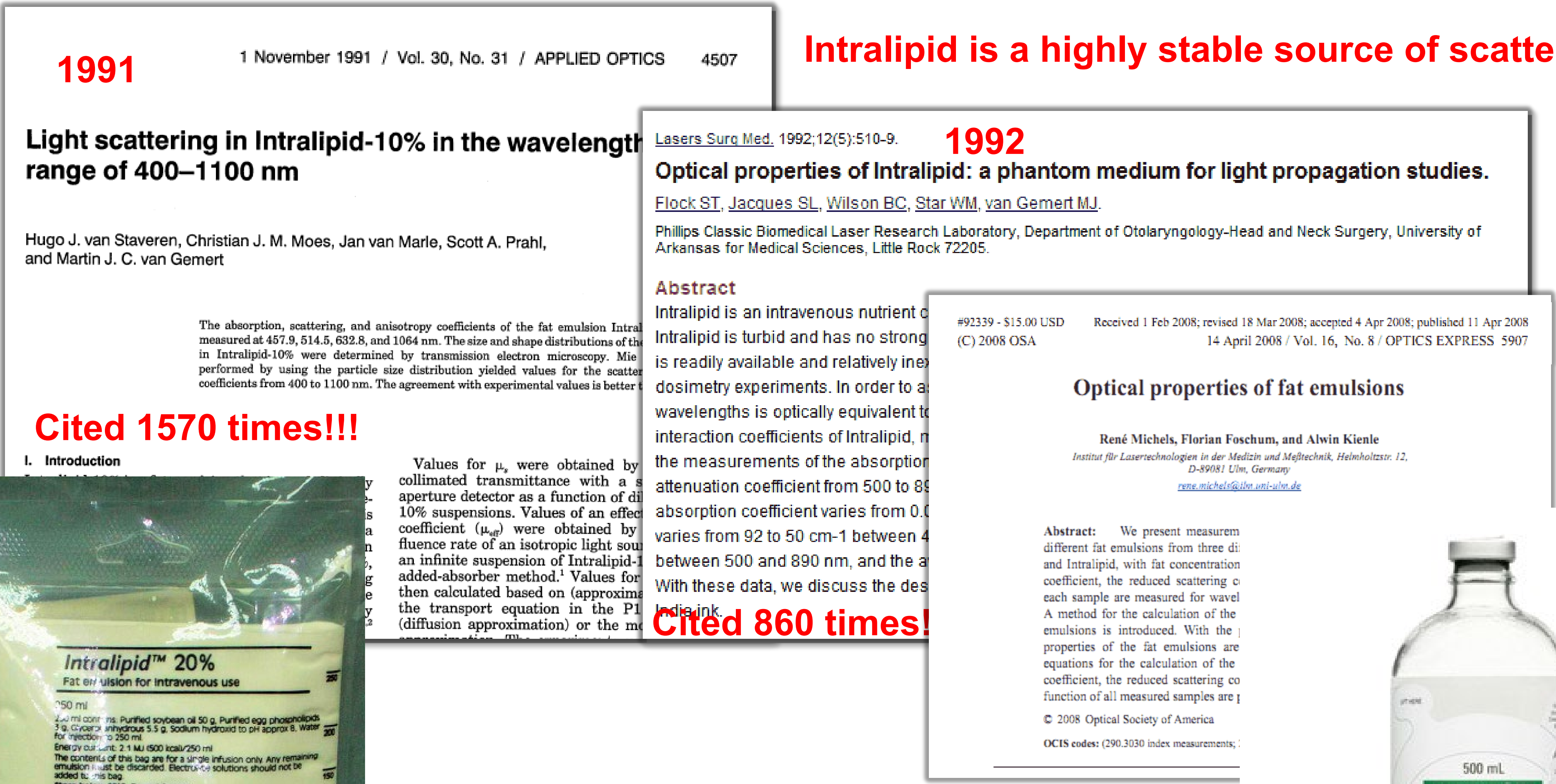






Intralipid is a highly stable source of scattering media

1991


1 November 1991 / Vol. 30, No. 31 / APPLIED OPTICS 4507

Light scattering in Intralipid-10% in the wavelength range of 400–1100 nm

Hugo J. van Staveren, Christian J. M. Moes, Jan van Marle, Scott A. Prahl, and Martin J. C. van Gemert

The absorption, scattering, and anisotropy coefficients of the fat emulsion Intral measured at 457.9, 514.5, 632.8, and 1064 nm. The size and shape distributions of the in Intralipid-10% were determined by transmission electron microscopy. Mie performed by using the particle size distribution yielded values for the scatter coefficients from 400 to 1100 nm. The agreement with experimental values is better t

I. Introduction

Values for μ_s were obtained by collimated transmittance with a s aperture detector as a function of di 10% suspensions. Values of an effec coefficient (μ_{eff}) were obtained by fluence rate of an isotropic light sou an infinite suspension of Intralipid-1 added-absorber method.[1] Values for then calculated based on (approxima the transport equation in the P1 (diffusion approximation) or the mo

Lasers Surg Med. 1992;12(5):510-9.

Optical properties of Intralipid: a phantom medium for light propagation studies.

Flock ST, Jacques SL, Wilson BC, Star WM, van Gemert MJ.

Phillips Classic Biomedical Laser Research Laboratory, Department of Otolaryngology-Head and Neck Surgery, University of Arkansas for Medical Sciences, Little Rock 72205.

Abstract

Intralipid is an intravenous nutrient c Intralipid is turbid and has no strong is readily available and relatively inex dosimetry experiments. In order to a wavelengths is optically equivalent to interaction coefficients of Intralipid, m the measurements of the absorption attenuation coefficient from 500 to 89 absorption coefficient varies from 0.0 varies from 92 to 50 cm-1 between 4 between 500 and 890 nm, and the a With these data, we discuss the des India ink.

#92339 - $15.00 USD Received 1 Feb 2008; revised 18 Mar 2008; accepted 4 Apr 2008; published 11 Apr 2008
(C) 2008 OSA 14 April 2008 / Vol. 16, No. 8 / OPTICS EXPRESS 5907

Optical properties of fat emulsions

René Michels, Florian Foschum, and Alwin Kienle

Institut für Lasertechnologien in der Medizin und Meßtechnik, Helmholtzstr. 12, D-89081 Ulm, Germany

rene.michels@ilm.uni-ulm.de

Abstract: We present measurem different fat emulsions from three di and Intralipid, with fat concentration coefficient, the reduced scattering c each sample are measured for wavel A method for the calculation of the emulsions is introduced. With the properties of the fat emulsions are equations for the calculation of the coefficient, the reduced scattering co function of all measured samples are

© 2008 Optical Society of America

OCIS codes: (290.3030 index measurements;

Cited 1570 times!!!

1992

Cited 860 times!

6 types

Intralipid® (Fresenius Kabi AB, Uppsala Sweden)
Nutralipid ® (Pharmicia, Quebec),
Liposyn ® I, II, III (Abbot Labs, Montreal)

Baxter

Urgent Product Recall

March 11, 2008

RE: INTRALIPID IV Fat Emulsions

Dear Director of Pharmacy:

Due to reports of leaking, Baxter Healthcare, the sole distributor of INTRALIPID IV Fat Emulsions is issuing a voluntary recall for its manufacturer, Fresenius Kabi, for the following INTRALIPID IV Fat Emulsion product codes, identified with the following lot numbers:

2008

Hospira Issues Nationwide Voluntary Recall of Certain Lots of Liposyn™ and Propofol Products That May Contain Particulate Matter

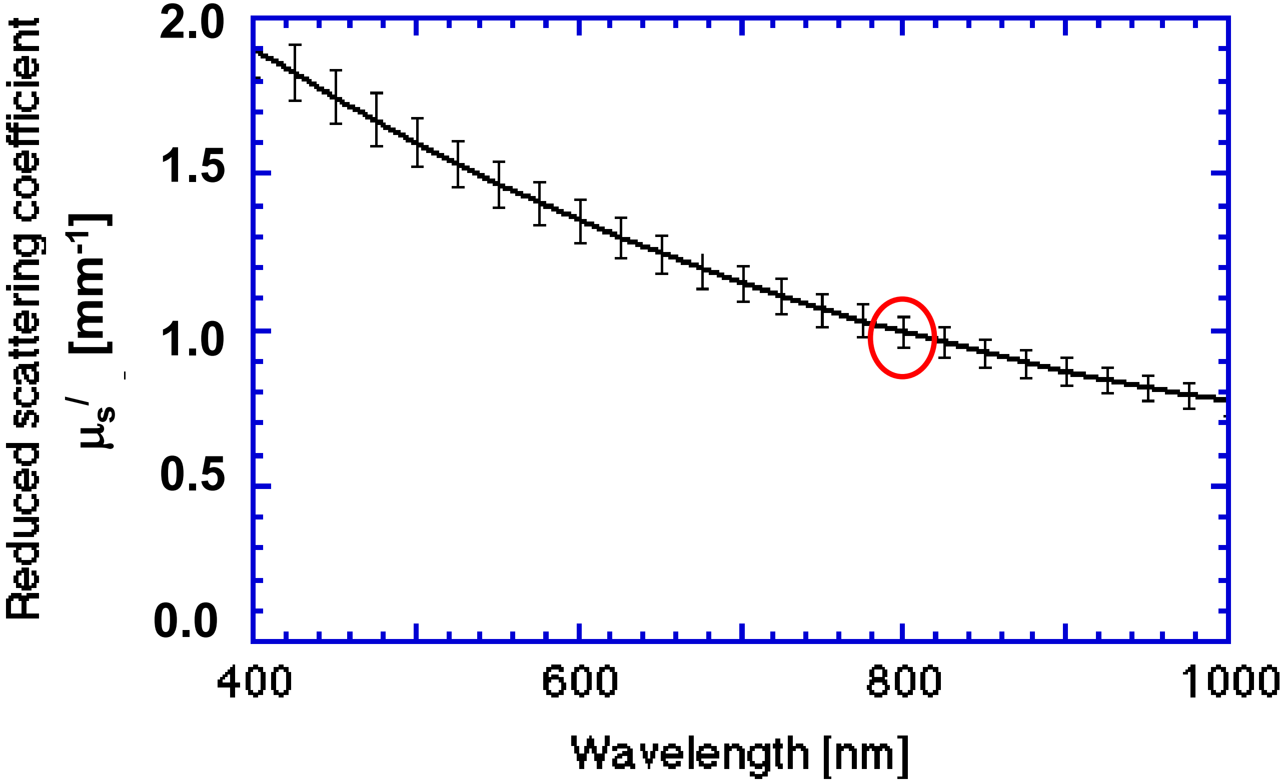
Nov. 6, 2009 - Lake Forest, Ill. - Hospira, Inc. (NYSE: HSP),, is voluntarily recalling 85 lots of Liposyn™ II 10%, Liposyn II 20%, Liposyn III 10%, Liposyn III 20%, Liposyn III 30% and 73 lots of Propofol Injectable Emulsion 1% … because some of the containers may contain particulate matter. The source of the particulate matter has been identified as stainless steel equipment used in the manufacturing process.

Cost $50/Liter c1990 → → → $1000/Liter c2010

Scattering spectrum of 1% Intralipid

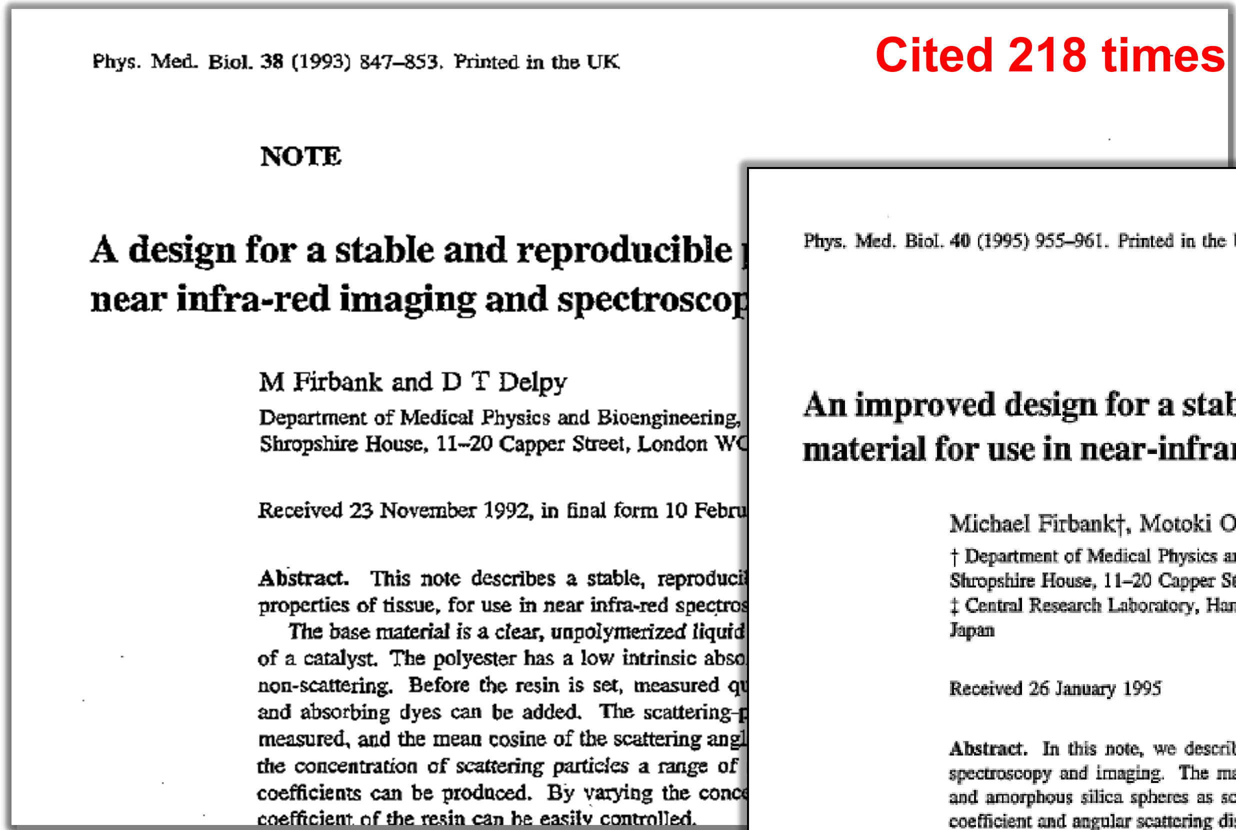
$$\mu_s'(\lambda) = A\,\lambda^{-b}$$

A – amplitude
b – scattering power
b = 1.4



$\mu_s' = 1.0\ mm^{-1}$ at 800 nm

c1993-1995



Phys. Med. Biol. 38 (1993) 847–853. Printed in the UK

NOTE

A design for a stable and reproducible p
near infra-red imaging and spectroscop

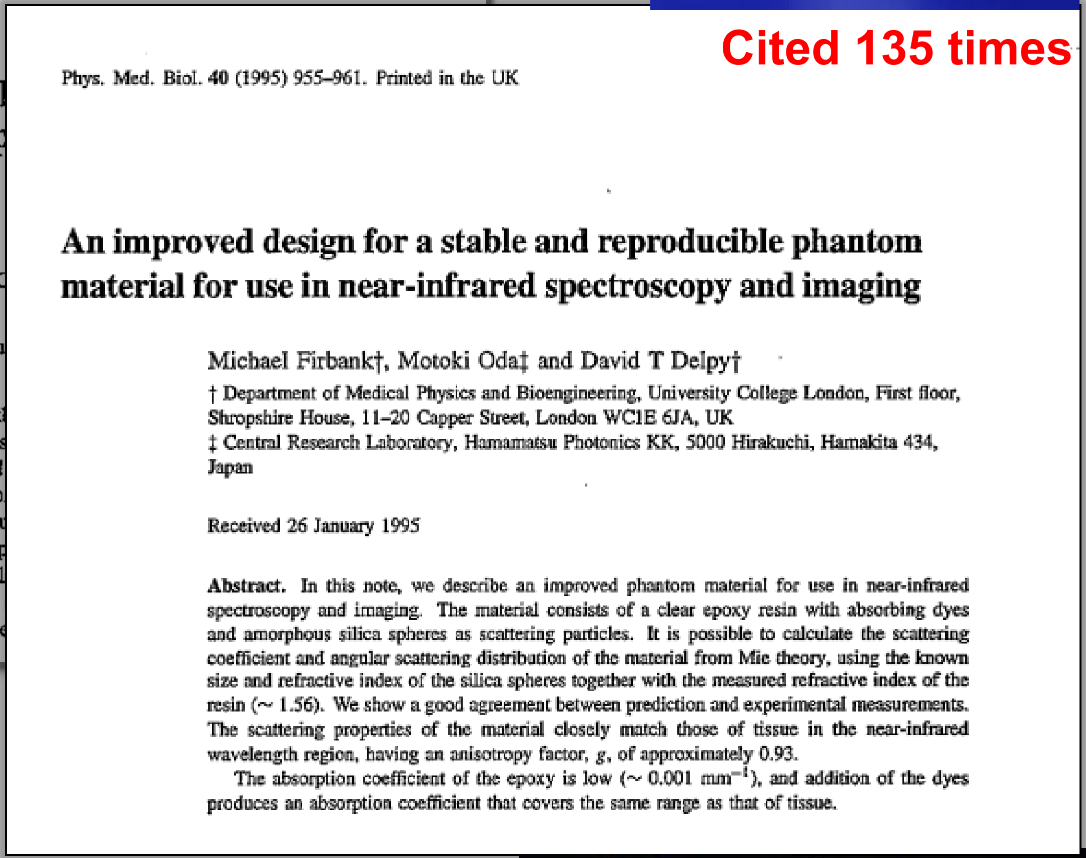
M Firbank and D T Delpy
Department of Medical Physics and Bioengineering,
Shropshire House, 11–20 Capper Street, London WC

Received 23 November 1992, in final form 10 Febru

Abstract. This note describes a stable, reproduci
properties of tissue, for use in near infra-red spectros
The base material is a clear, unpolymerized liquid
of a catalyst. The polyester has a low intrinsic abso
non-scattering. Before the resin is set, measured qu
and absorbing dyes can be added. The scattering-p
measured, and the mean cosine of the scattering angl
the concentration of scattering particles a range of
coefficients can be produced. By varying the conce
coefficient of the resin can be easily controlled.

Cited 218 times

Cited 135 times



Phys. Med. Biol. 40 (1995) 955–961. Printed in the UK

An improved design for a stable and reproducible phantom material for use in near-infrared spectroscopy and imaging

Michael Firbank†, Motoki Oda‡ and David T Delpy†
† Department of Medical Physics and Bioengineering, University College London, First floor, Shropshire House, 11–20 Capper Street, London WC1E 6JA, UK
‡ Central Research Laboratory, Hamamatsu Photonics KK, 5000 Hirakuchi, Hamakita 434, Japan

Received 26 January 1995

Abstract. In this note, we describe an improved phantom material for use in near-infrared spectroscopy and imaging. The material consists of a clear epoxy resin with absorbing dyes and amorphous silica spheres as scattering particles. It is possible to calculate the scattering coefficient and angular scattering distribution of the material from Mie theory, using the known size and refractive index of the silica spheres together with the measured refractive index of the resin (~ 1.56). We show a good agreement between prediction and experimental measurements. The scattering properties of the material closely match those of tissue in the near-infrared wavelength region, having an anisotropy factor, g, of approximately 0.93.
The absorption coefficient of the epoxy is low (~ 0.001 mm^{-1}), and addition of the dyes produces an absorption coefficient that covers the same range as that of tissue.

UCL BORL Webpage

Components
Epoxy resin: Araldite epoxy (MY753) & hardener (XD716), mixed in ratio 3:1.
Supplier: Aeropia Chemical Supplies (Crawley, UK).
Near-infrared dye: Pro jet 900NP.
Supplier: Avecia (Manchester, UK), formally known as Zeneca Ltd.
Scatterer: "Superwhite" polyester pigment.
Supplier: Alec Tiranti Ltd. (London, UK).

Cited >1000 times

Journal of Biomedical Optics 11(4), 041102 (July/August 2006)

Review of tissue simulating phantoms for optical spectroscopy, imaging and dosimetry

Brian W. Pogue
Dartmouth College
Thayer School of Engineering
Hanover, New Hampshire 03755

Michael S. Patterson
Juravinski Cancer Center
Department of Medical Physics
Hamilton, Ontario, Canada
and
McMaster University
Hamilton, Ontario, Canada

Abstract. Optical spectroscopy, imaging, and therapy tissue phantoms must have the scattering and absorption properties that are characteristic of human tissues, and over the past few decades, many useful models have been created. In this work, an overview of their composition and properties is outlined, by separating matrix, scattering, and absorbing materials, and discussing the benefits and weaknesses in each category. Matrix materials typically are water, gelatin, agar, polyester or epoxy and polyurethane resin, room-temperature vulcanizing (RTV) silicone, or polyvinyl alcohol gels. The water and hydrogel materials provide a soft medium that is biologically and biochemically compatible with addition of organic molecules, and are optimal for scientific laboratory studies. Polyester, polyurethane, and silicone phantoms are essentially permanent matrix compositions that are suitable for routine calibration and testing of established systems. The most common three choices for scatters have been: (1.) lipid based emulsions, (2.) titanium or aluminum oxide powders, and (3.) polymer microspheres. The choice of absorbers varies widely from hemoglobin and cells for biological simulation, to molecular dyes and ink as less biological but more stable absorbers. This review is an attempt to indicate which sets of phantoms are optimal for specific applications, and provide links to studies that characterize main phantom material properties and recipes. [DOI: 10.1117/1.2335429]

Keywords: tissue simulating phantoms; optical spectroscopy; imaging; dosimetry.

Paper 05287SSR received Sep. 30, 2005; revised manuscript received Jan. 10, 2006; accepted for publication Jan. 11, 2006; published online Sep. 1, 2006.

1 Introduction

1.1 *Medical Tissue-Simulating Phantoms*

for minimum performance criteria for new systems and for routine monitoring of existing systems. The benefit of this procedure is that system performance can then be made more

Journal of Biomedical Optics 11(4), 041102 (July/August 2006)

Review of tissue simulating phantoms for optical spectroscopy, imaging and dosimetry

scatterers

Typically ‘white’
Highly pure or concentrated
Highly available
Inexpensive
Mie or Rayleigh scatterers

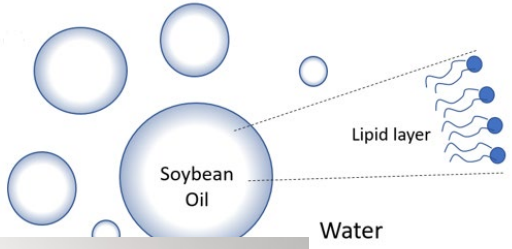
absorbers

Typically ‘pigmented’
Highly pure or concentrated
Highly available
Inexpensive
Matching tissue absorption

Options for Scattering particles

Scattering Material	Perm-anent ?	Particle Size [nm]	Index of refraction	Particle distribution function	Recommended Use
Lipids					
Polymer microspheres					
TiO_2 Al_2O_3 Powders					
Quartz glass microspheres					

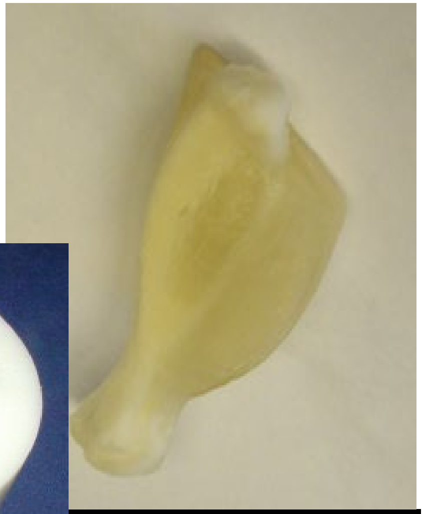
Intralipid particles

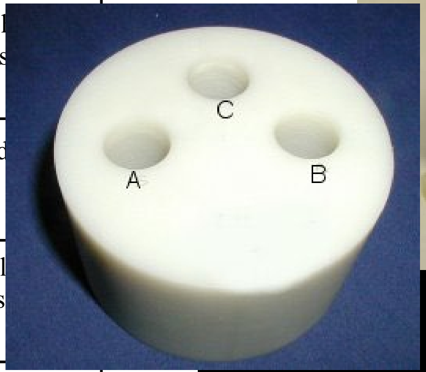


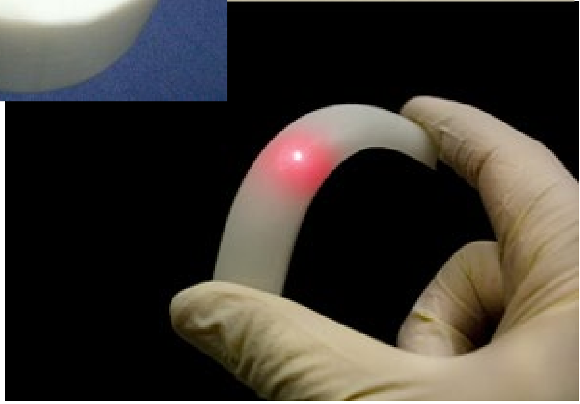
Pogue & Patterson, J. Biomed Opt. 2006

Phantom Matrix Materials

Phantom Matrix Material	Permanent ?	Solid/ Liquid/ Flexible	Biologically Compatible	Organic Chemical Compatible	Index of refraction	Recommended Use
Aqueous suspension	Y/N	L	Y	Y	1.34	Initial use & multiple phantom contrast studies
Gelatin/Agar matrix	N	F	Y	Y	1.35	Detailed heterogeneity pl studies bio-absorbers fluorophores
Polyacrylamide gel	N	F	Y	Y	1.35	Thermal therapy stud
Polyester or Epoxy Resin	Y	S	N	N	1.54	Calibration & routine val Intersystem comparis
Polyurethane Resin	Y	S	N	N/Y	1.50	Calibration & routine validation Intersystem comparisons Inclusion of dyes
RTV Silicone	Y	F	N	N	1.4	Complex geometries with permanent flexible phantoms

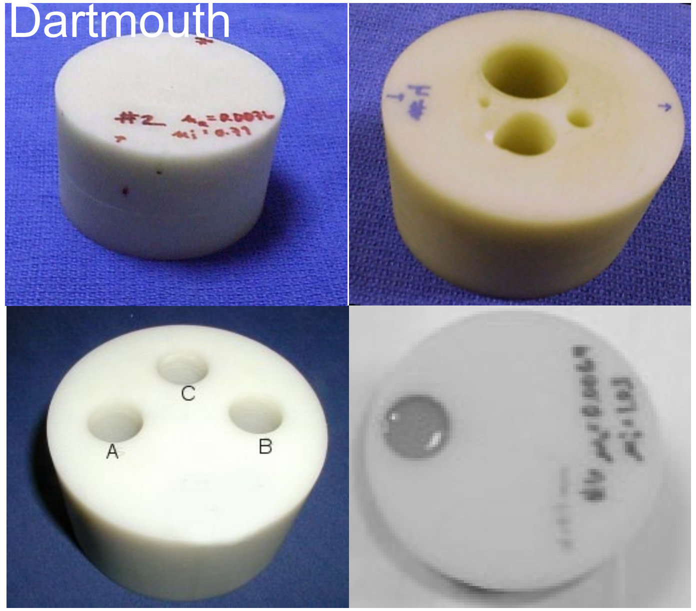


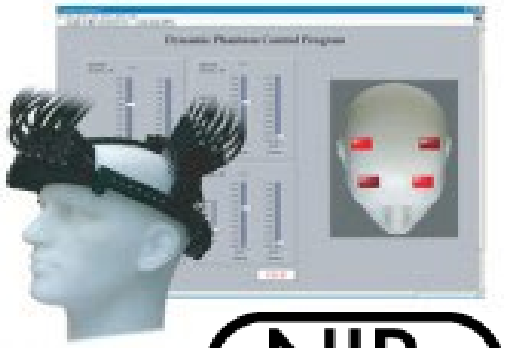




Pogue & Patterson, J. Biomed Opt. 2006

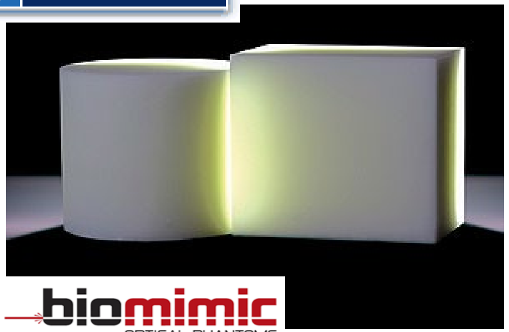
Solid phantoms





NIRx
MEDICAL TECHNOLOGIES

INO



biomimic
OPTICAL PHANTOMS

Caliper LifeSciences

Silicone Rubber base:

better contact & mechanical tissue simulation

Lasers in Surgery and Medicine 21:227–234 (1997)

Three-Dimensional Optical Phantom and Its Application in Photodynamic Therapy

Roland Bays, PhD,[1*] Georges Wagnières, PhD,[1] Dimitri Robert, BS,[1]
Jean-François Theumann, PhD,[1] Alex Vitkin, PhD,[3] Jean-François Savary, MD,[2]
Philippe Monnier, MD,[2] and Hubert van den Bergh, PhD[1]

[1]Institute of Environmental Engineering, Swiss Federal Institute of Technology, CH-1015 Lausanne, Switzerland
[2]ENT Department, CHUV Hospital, CH-1011 Lausanne, Switzerland
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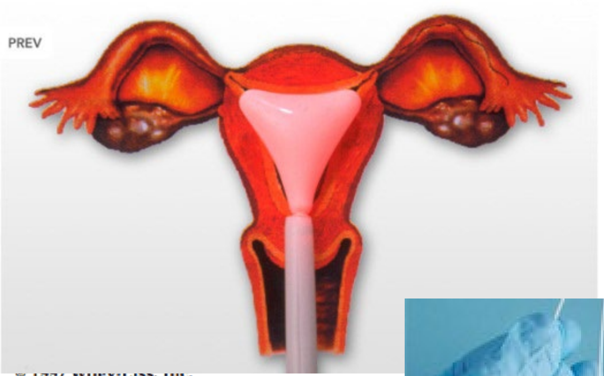
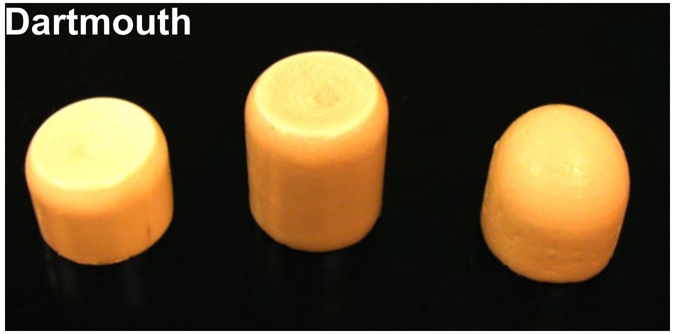
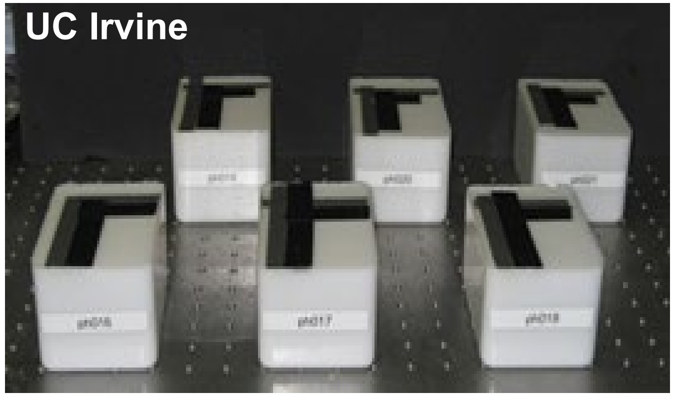
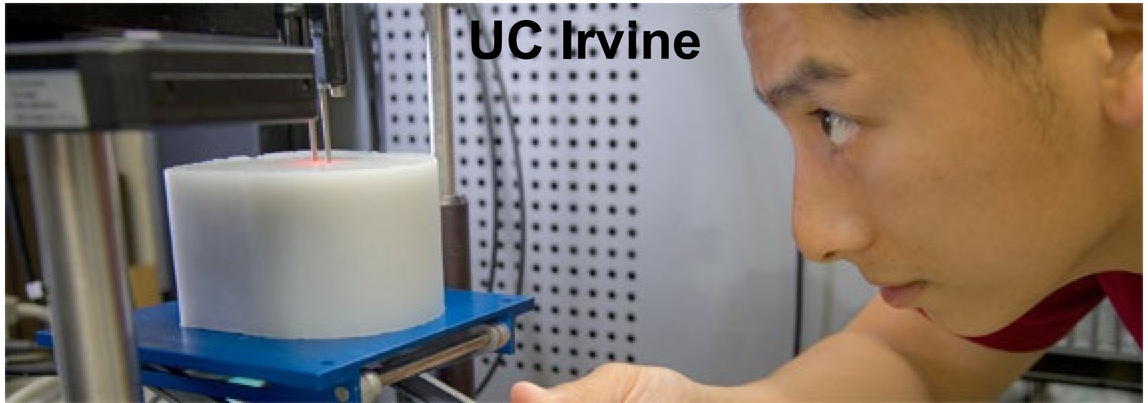


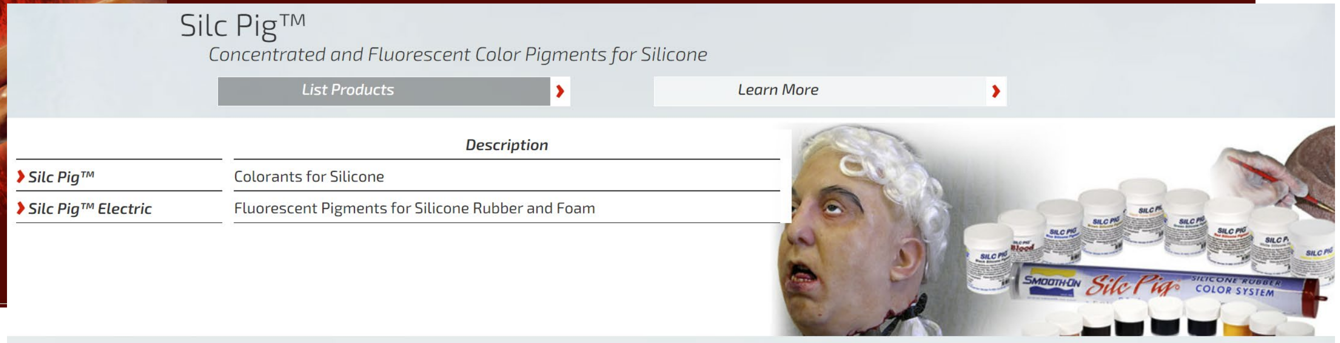
Medlight SA
PDT delivery







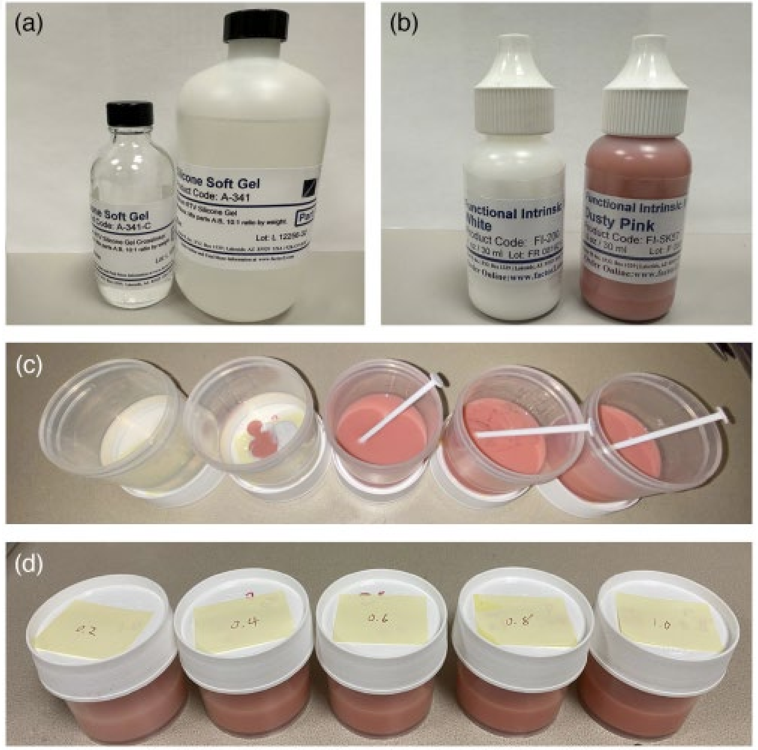
Commercially available option from your favorite Zombie movie: Smooth-On

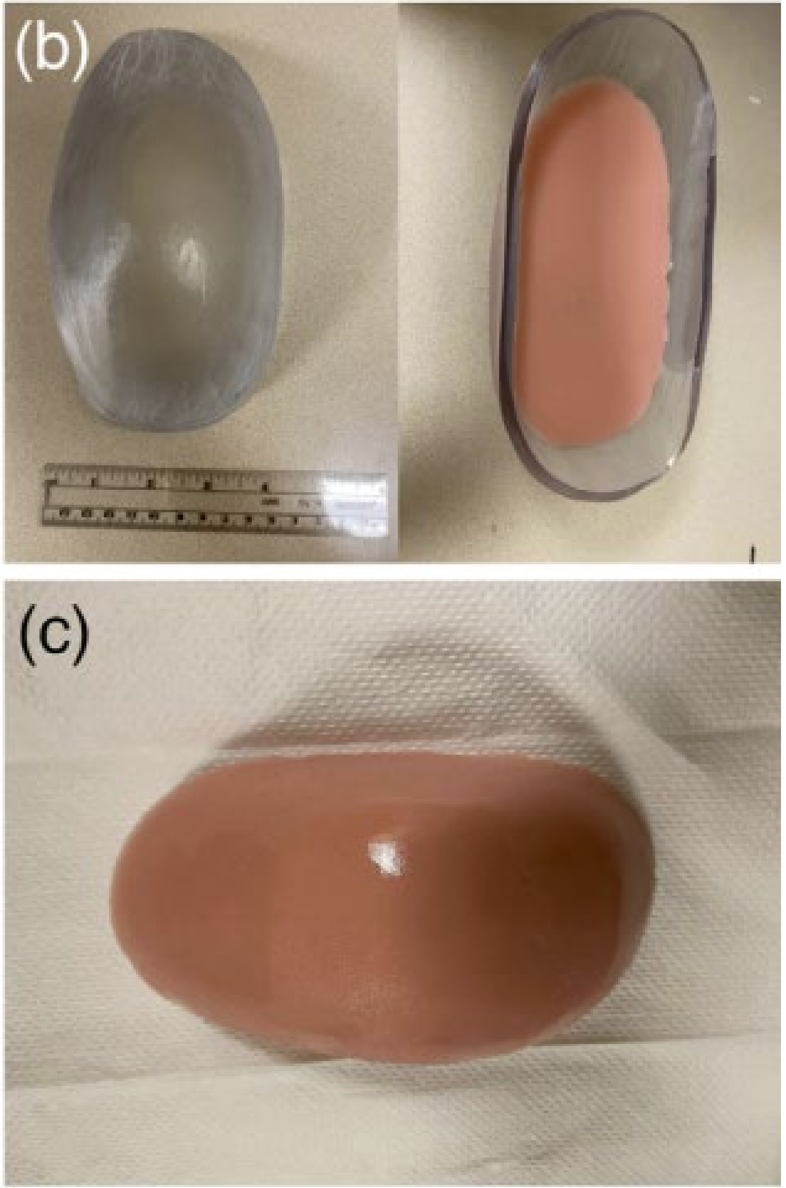


JBO Journal of Biomedical Optics

Stable tissue-mimicking phantoms for longitudinal multimodality imaging studies that incorporate optical, CT, and MRI contrast

Mengyang Zhao,[a] Mingwei Zhou,[a] Xu Cao,[a] Jinchao Feng,[b] Brian W. Pogue,[a,†] Keith D. Paulsen,[a] and Shudong Jiang[a,*]
[a]Dartmouth College, Thayer School of Engineering, Hanover, New Hampshire, United States
[b]Beijing University of Technology, Beijing Key Laboratory of Computational Intelligence and Intelligent System, Faculty of Information Technology, Beijing, China





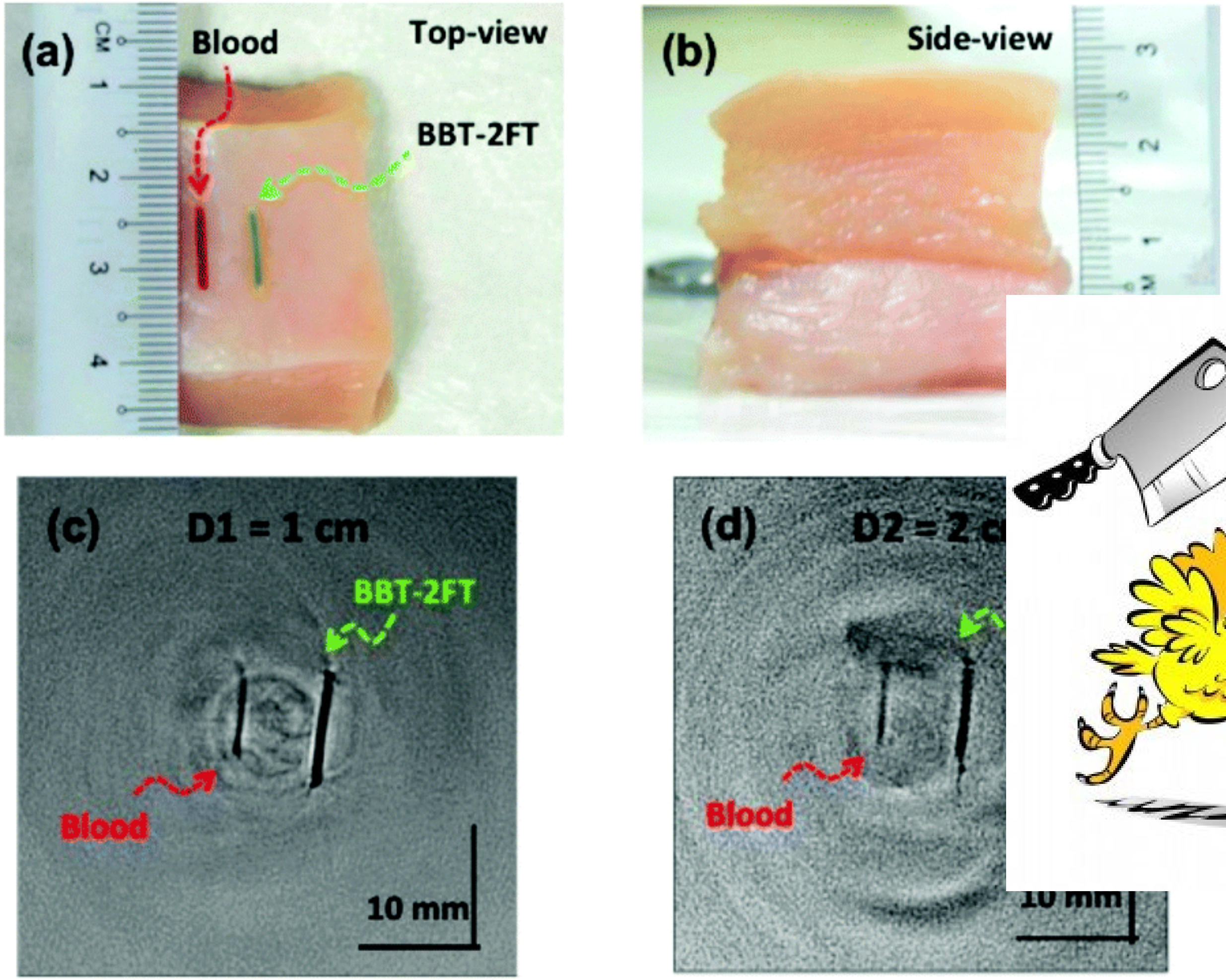
1% white
0.5% pink

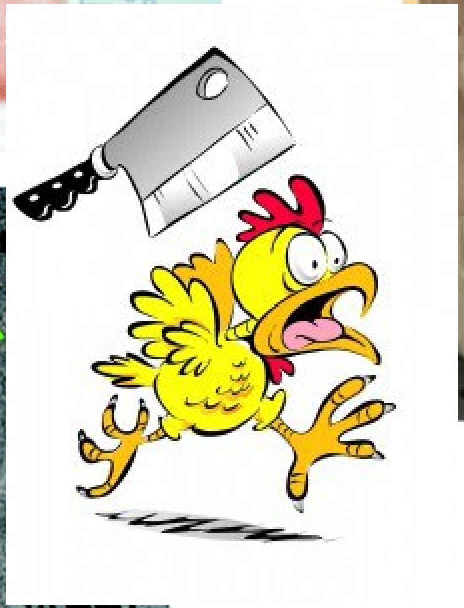
98.5% silicone

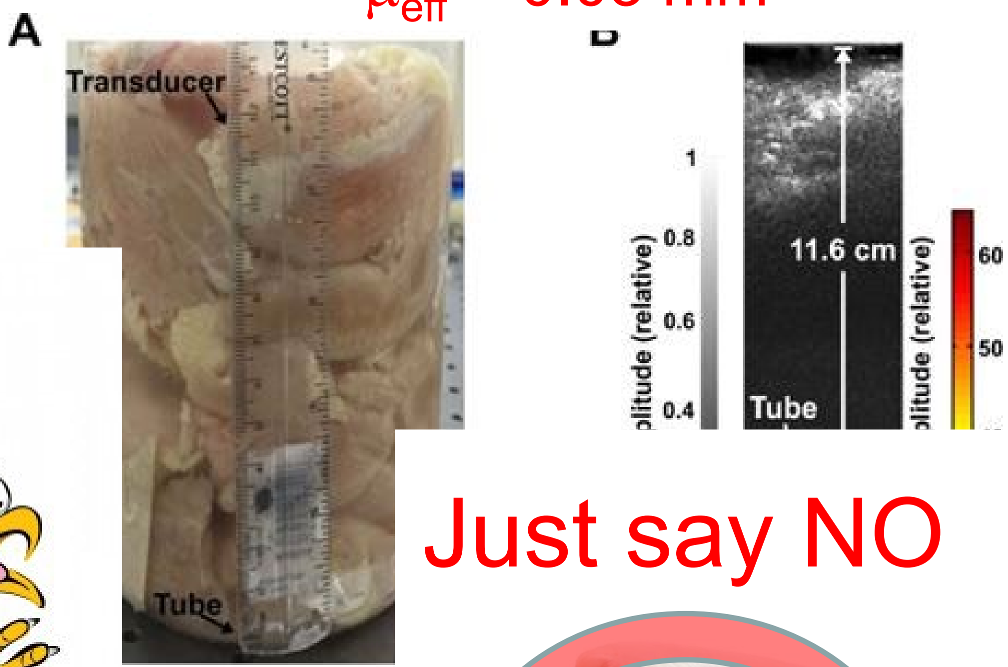
The tricky choice: Chicken breast → very low scatter!

μ_a = 0.003 mm^{-1}, μ_s' = 0.3 mm^{-1}

μ_{eff} = 0.03 mm^{-1}







Just say NO

Anonymous….

Biologically compatible optical phantoms?

Biological/Biochemical Phantom additives – typically aqueous

Additives	Function	Limitations	Stability
EDTA Penicillin	To avoid bacterial growth		Days - Weeks
Yeast or Sodium azide	Remove molecular oxygen		Hours
Formaldehyde	Increase melting temperature above room temp.		Years
Whole Blood	Provide realistic tissue spectra	Oxygen saturation is not easily changed	Days
Ink	Provide flat absorption spectra	- Not stable nor repeatable unless highly calibrated	Days – Years
Organic molecules (i.e. glucose)	Matrix holds most organic compounds	- stability of each molecule must be assessed	Days
Fluorophores	-Compatible with aqueous - Gelatin provides some de-aggregation	- May need to avoid aggregation effects with addition of additional agents	Days – Weeks
Heterogeneities	- Test Tomography and Imaging capabilities - Inclusions can be liquid or solid	- Clear enclosures need to be avoided due to light channeling - Index changes significantly at inclusions	Days – Weeks
Gadolinium or Copper Sulphate	Provide varying levels of Magnetic resonance contrast		Years
Actinometry agents	Provide measure of photochemical dose de	Unstable over long periods of time	Hours

Pogue & Patterson, J. Biomed Opt. 2006

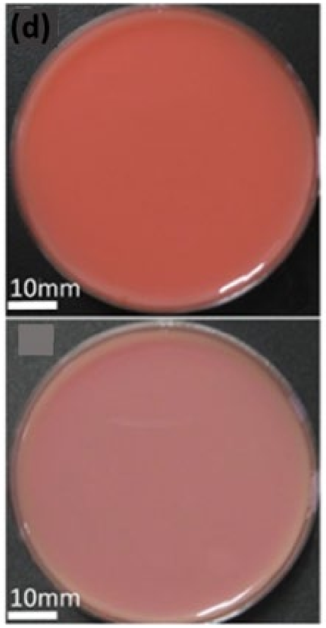
Gelatin/Agar Base

Gelatin / agar

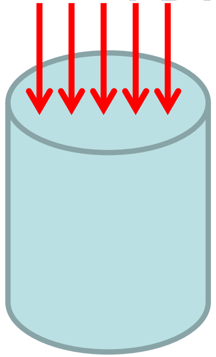
with TiO2 scatter

with blood

varying blood %

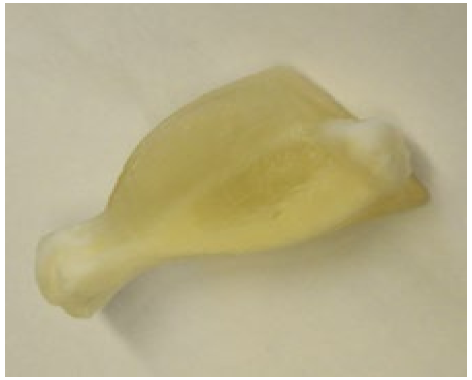


Chemical actinometry
PDT Dosimetry



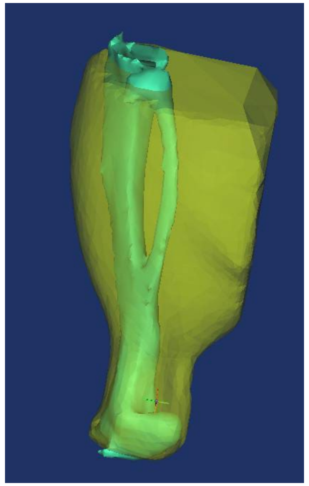
Gelatin
TiO2
ink
dichloroflorescien

Bone embedded



Leg/Arm Phantoms for shape & biochemistry

for Raman Tomography of bone mineral

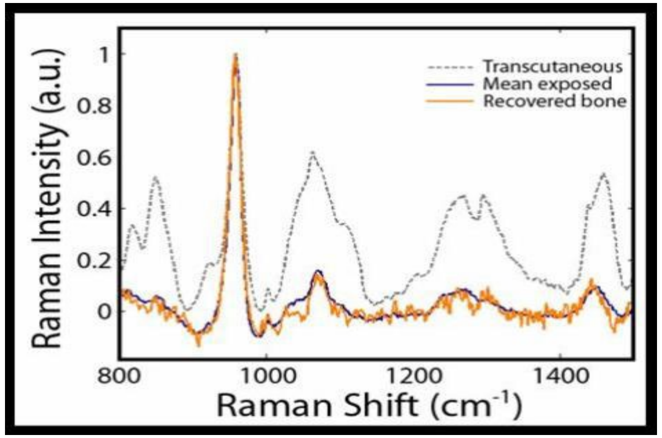


Gelatin over bone

Rat tibia phantom

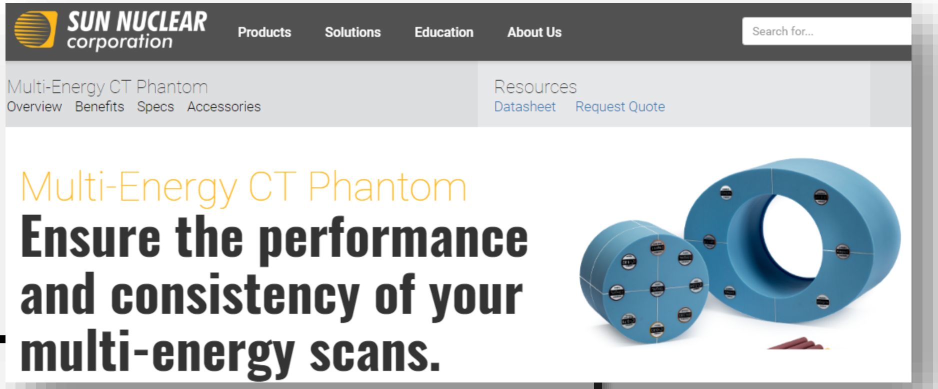
Anthropomorphic Mouse

CT scan → mold cast



Courtesy: Esmonde-White et al, Analyst, 2011

Phantoms are big business in medical imaging



Where can you get blood?

LAMPIRE BIOLOGICAL LABORATORIES

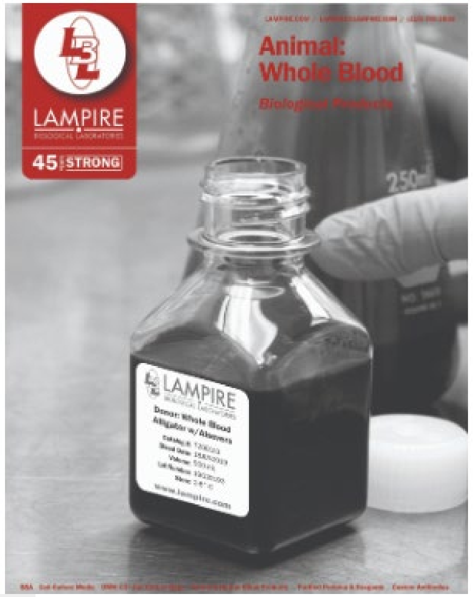
Many suppliers: just Google: research blood suppliers…

Part #	Species	Breed	Item Type	Anticoagulant	Gender	Volume	Price
7200103	Alligator		WHOLE BLOOD	Alsevers		500 ml	$650.00
7200103	Alligator		WHOLE BLOOD	Alsevers		1,000 ml	$1,177.00
7200501	Canine	BEAGLE	WHOLE BLOOD	ACD		50 ml	$434.00
7200501	Canine	BEAGLE	WHOLE BLOOD	ACD		100 ml	$619.00
7200801	Bovine		WHOLE BLOOD	ACD		50 ml	$33.00
7200801	Bovine		WHOLE BLOOD	ACD		100 ml	$50.00
7201401	Chicken		WHOLE BLOOD	ACD		50 ml	$81.00
7202101	Donkey		WHOLE BLOOD	ACD		50 ml	$33.00
7202203	Emu		WHOLE BLOOD	Alsevers		50 ml	$600.00
7202511	Goat		WHOLE BLOOD	NA HEPARIN		500 ml	$87.00
7203401	Horse		WHOLE BLOOD	ACD		50 ml	$33.00
7206401	Rabbit		WHOLE BLOOD	ACD		50 ml	$360.00

Species Available:

- Alligator
- Bovine
- Calf
- Chicken
- Donkey
- Emu
- Goat
- Goose
- Guinea Pig
- Hamster
- Horse
- Llama
- Mouse
- Primate
- Porcine
- Rabbit
- Rat
- Rooster
- Sheep
- Trout
- Turkey

(Other Species Available, Please Inquire)

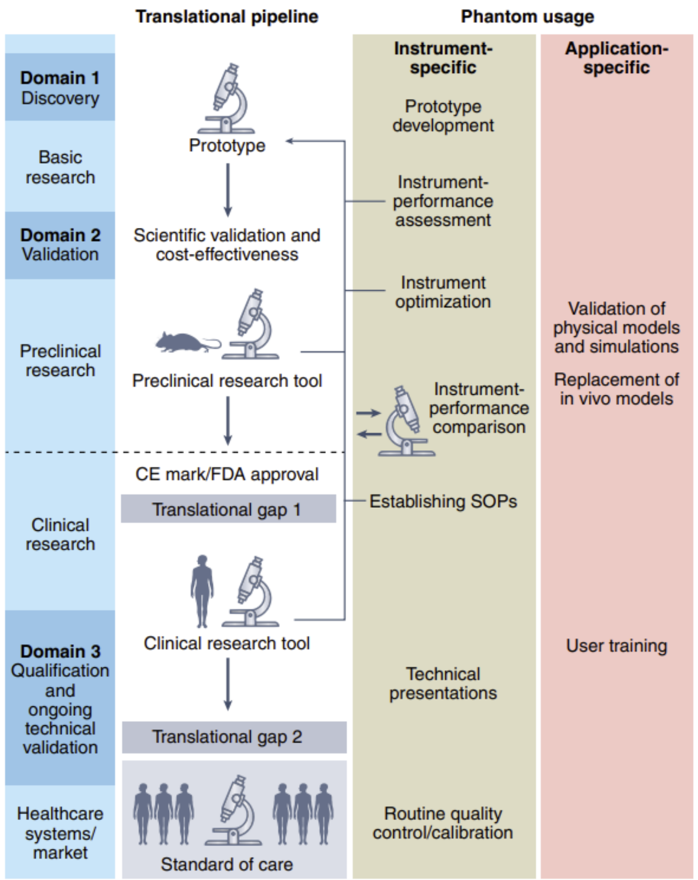


Efforts on Standardization

nature biomedical engineering
PERSPECTIVE
https://doi.org/10.1038/s41551-022-00890-6
Check for updates

Criteria for the design of tissue-mimicking phantoms for the standardization of biophotonic instrumentation

Lina Hacker[1,2], Heidrun Wabnitz[3], Antonio Pifferi[4], T. Joshua Pfefer[5], Brian W. Pogue[6] and Sarah E. Bohndiek[1,2] ✉



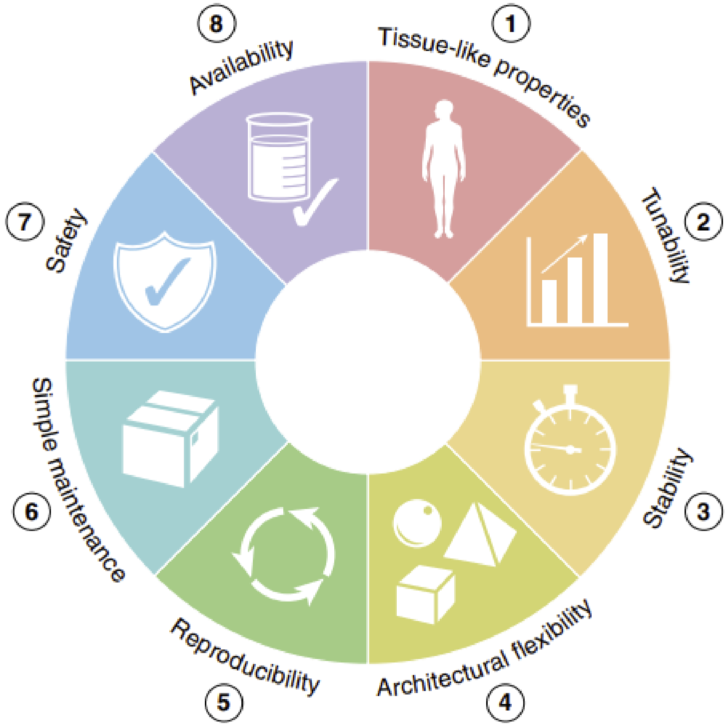
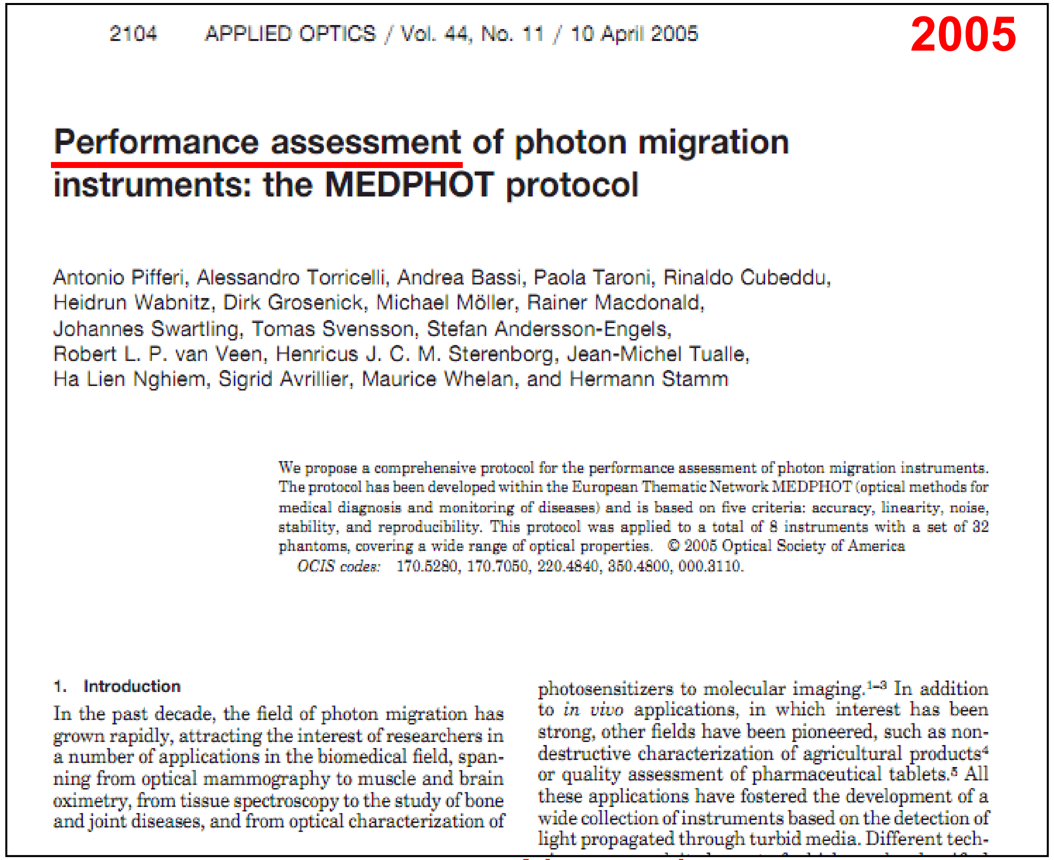


Table 3 | Comparison of the properties of materials used for biophotonic phantoms

	Tissue-mimicking properties			Handling properties			Fabrication properties			Biocompatibility	Refs.
Material	Optical	Acoustic	Tunability	Temporal stability	Mechanical stability	Storage and transport	Architectural flexibility	Complexity	Safety		
Aqueous suspension	++	–	+	– –	– –	– –	–	++	++	Yes	43,284
Agar/gelatin	++	++	++	–	–	–	++	++	++	Yes	47,48,51,52,78,79,82,285
Polyacrylamide	++	++	++	–	+	–	++	+	–	Yes	96
PVA	++	++	++	+	+	–	++	–	++	Yes	88,90,105,286,287
Co-polymer in oil	++	+	+	++	++	++	++	+	++	No	166–168
PVCP	++	+	+	++	++	++	+	+	+	No	95,154,156
Silicone	++	-	+	++	++	++	++	+	++	No	131,132,272
Polyurethane	++	+	+	++	++	++	++	+	+	No	27,46,116
Polyester, epoxy resin	++	– –	+	++	++	++	+	+	++	No	35,108,109,120
Ex vivo tissues	++	++	– –	–	++	–	– –	++	++	Yes	5

++, excellent performance; +, above-average performance; –, below-average performance; – –, poor performance.

Standardization between EU systems



2104 APPLIED OPTICS / Vol. 44, No. 11 / 10 April 2005

2005

Performance assessment of photon migration instruments: the MEDPHOT protocol

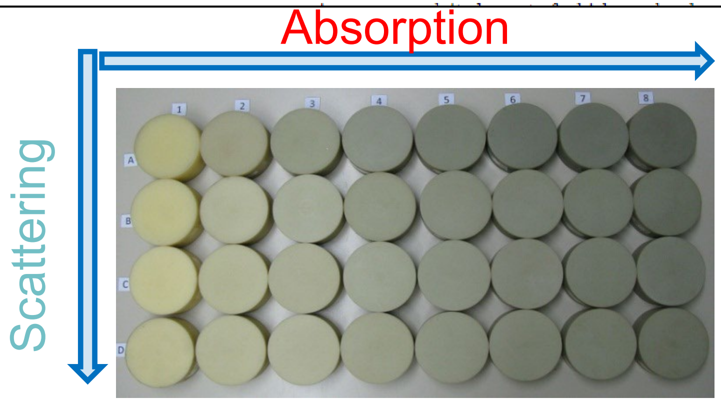
Antonio Pifferi, Alessandro Torricelli, Andrea Bassi, Paola Taroni, Rinaldo Cubeddu, Heidrun Wabnitz, Dirk Grosenick, Michael Möller, Rainer Macdonald, Johannes Swartling, Tomas Svensson, Stefan Andersson-Engels, Robert L. P. van Veen, Henricus J. C. M. Sterenborg, Jean-Michel Tualle, Ha Lien Nghiem, Sigrid Avrillier, Maurice Whelan, and Hermann Stamm

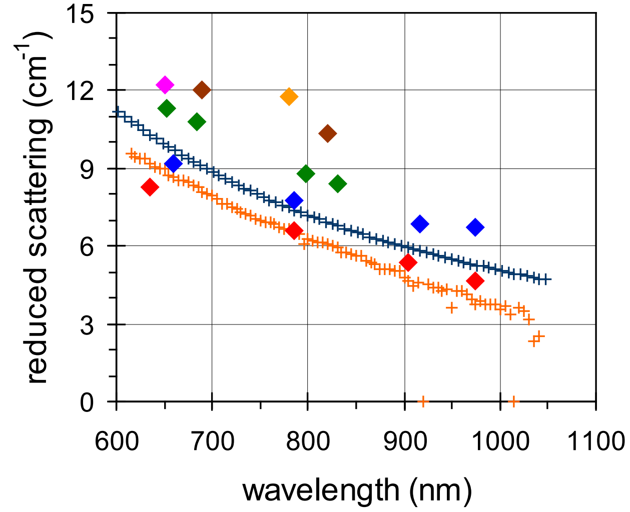
We propose a comprehensive protocol for the performance assessment of photon migration instruments. The protocol has been developed within the European Thematic Network MEDPHOT (optical methods for medical diagnosis and monitoring of diseases) and is based on five criteria: accuracy, linearity, noise, stability, and reproducibility. This protocol was applied to a total of 8 instruments with a set of 32 phantoms, covering a wide range of optical properties.

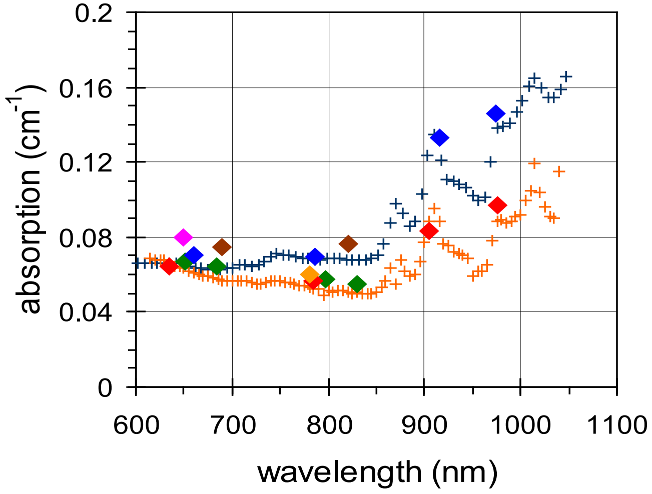
OCIS codes: 170.5280, 170.7050, 220.4840, 350.4800, 000.3110.

1. Introduction

In the past decade, the field of photon migration has grown rapidly, attracting the interest of researchers in a number of applications in the biomedical field, spanning from optical mammography to muscle and brain oximetry, from tissue spectroscopy to the study of bone and joint diseases, and from optical characterization of photosensitizers to molecular imaging.[1–3] In addition to *in vivo* applications, in which interest has been strong, other fields have been pioneered, such as nondestructive characterization of agricultural products[4] or quality assessment of pharmaceutical tablets.[5] All these applications have fostered the development of a wide collection of instruments based on the detection of light propagated through turbid media. Different tech-







Note: accuracy ± 20% is normal

Fluorescence guided surgery standardization

Journal of Biomedical Optics 22(1), 016009 (January 2017)

Benchmarking of fluorescence cameras through the use of a composite phantom

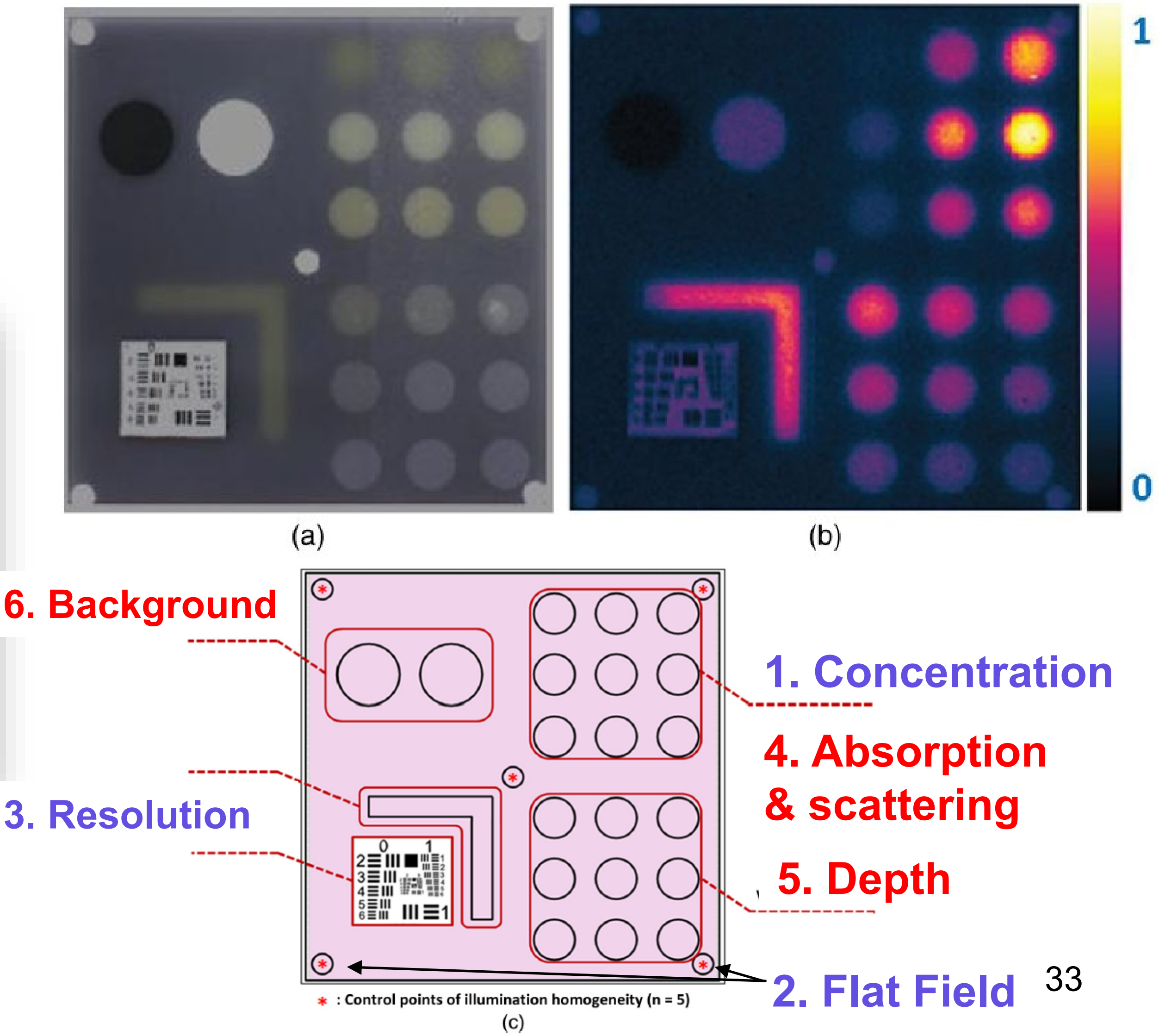
Dimitris Gorpas,[a,b] Maximilian Koch,[a,b] Maria Anastasopoulou,[a,b] Uwe Klemm,[b] and Vasilis Ntziachristos[a,b,*]
[a]Technical University Munich, Chair for Biological Imaging, Arcisstrasse 21, Munich D-80333, Germany
[b]Helmholtz Zentrum München, Institute for Biological and Medical Imaging, Ingolstädter Landstrasse 1, Neuherberg D-85764, Germany

Journal of Biomedical Optics 21(9), 091309 (September 2016)

Comprehensive phantom for interventional fluorescence molecular imaging

Maria Anastasopoulou,[a,b] Maximilian Koch,[a,b] Dimitris Gorpas,[a,b] Angelos Karlas,[a,b] Uwe Klemm,[a] Pilar Beatriz Garcia-Allende,[a,b] and Vasilis Ntziachristos[a,b,*]
[a]Helmholtz Zentrum München, Institute for Biological and Medical Imaging, Ingolstädter Landstraße 1, Neuherberg D-85764 Germany
[b]Technical University Munich, Chair for Biological Imaging, Arcisstraße 21, Munich D-80333, Germany

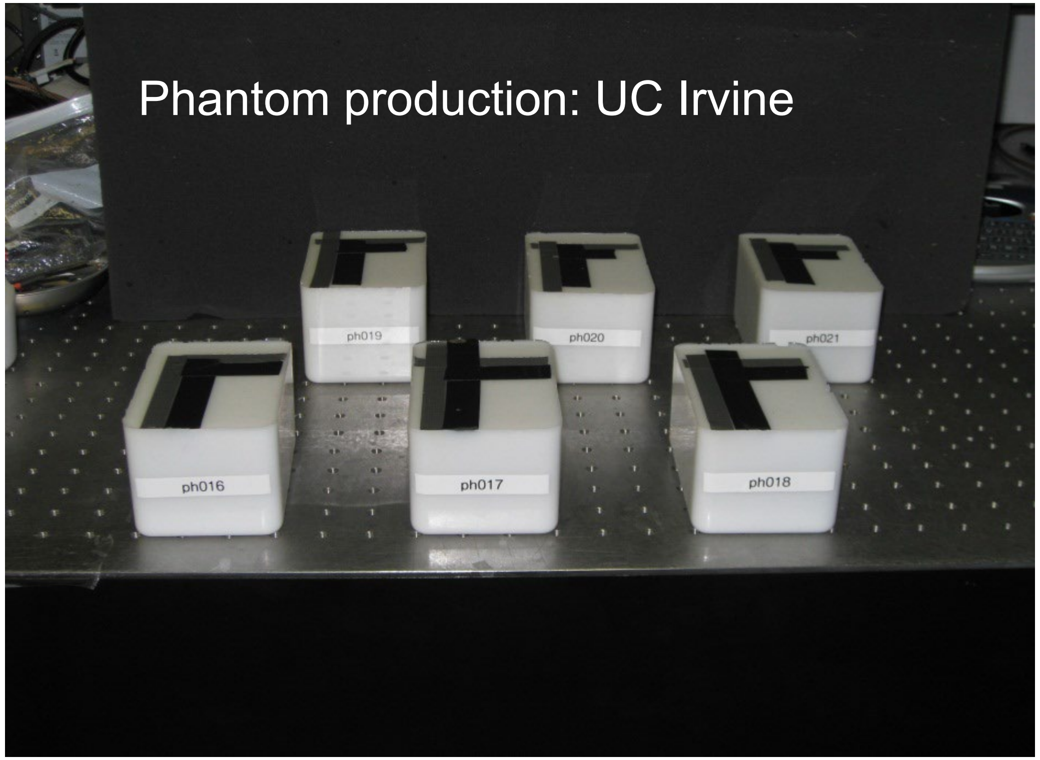
Abstract. Fluorescence imaging has been considered for over a half-century as a modality that could assist surgical guidance and visualization. The administration of fluorescent molecules with sensitivity to disease bio-markers and their imaging using a fluorescence camera can outline pathophysiological parameters of tissue invisible to the human eye during operation. The advent of fluorescent agents that target specific cellular responses and molecular pathways of disease has facilitated the intraoperative identification of cancer with improved sensitivity and specificity over nonspecific fluorescent dyes that only outline the vascular system and enhanced permeability effects. With these new abilities come unique requirements for developing phantoms to calibrate imaging systems and algorithms. We briefly review herein progress with fluorescence phantoms employed to validate fluorescence imaging systems and results. We identify current limitations and discuss



NIR spectroscopy - Multicenter clinical trials

ACRIN™
AMERICAN COLLEGE OF
RADIOLOGY
IMAGING NETWORK

5 sites in
Multicenter trial



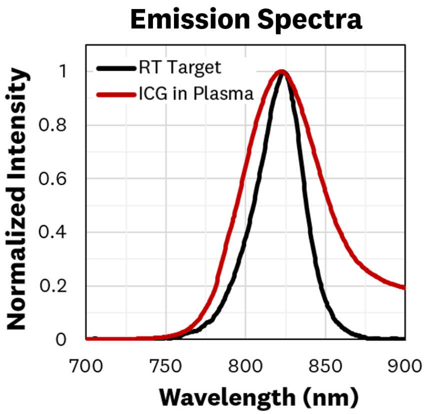
Standardization/commercialization effort
3D printed fluorescent phantoms

QUEL IMAGING

3D printed fluorescent test targets & phantoms

Ethan LaRochelle, PhD
CEO, Co-founder

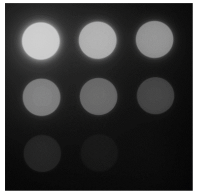
Alberto Ruiz
CTO, Co-founder

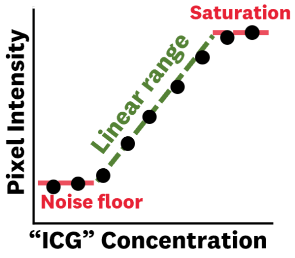


Concentration Sensitivity

1 – 1000 nM ICG-equivalent
+ control well (0 nM)

Fluorescence Image

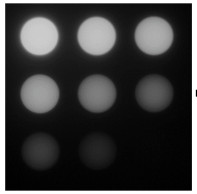


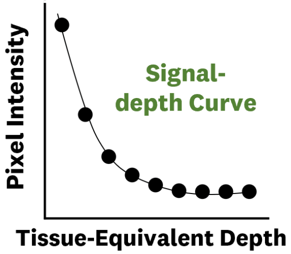


Depth Sensitivity

0.5 – 6.0 mm Tissue equivalent depths
@ 1000 nM ICG-equivalent

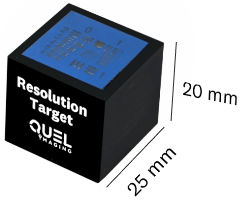
Fluorescence Image



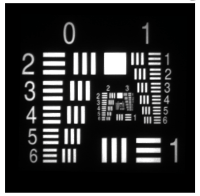


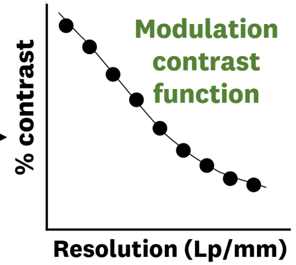
Fluorescence Resolution

USAF 1951 Resolution target
288 lp/mm (~2 μm) @ 1000 nM

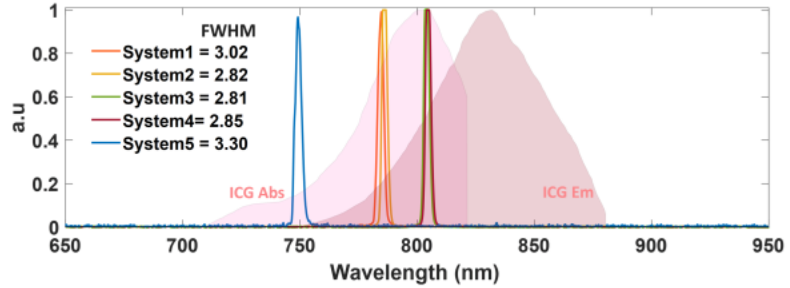


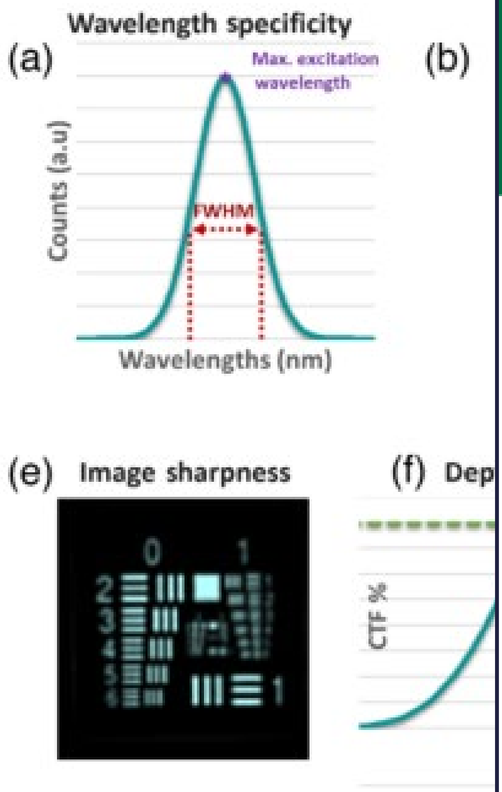
Fluorescence Image





UNIVERSITY OF WISCONSIN–MADISON





JBO Journal of Biomedical Optics

RESEARCH PAPER

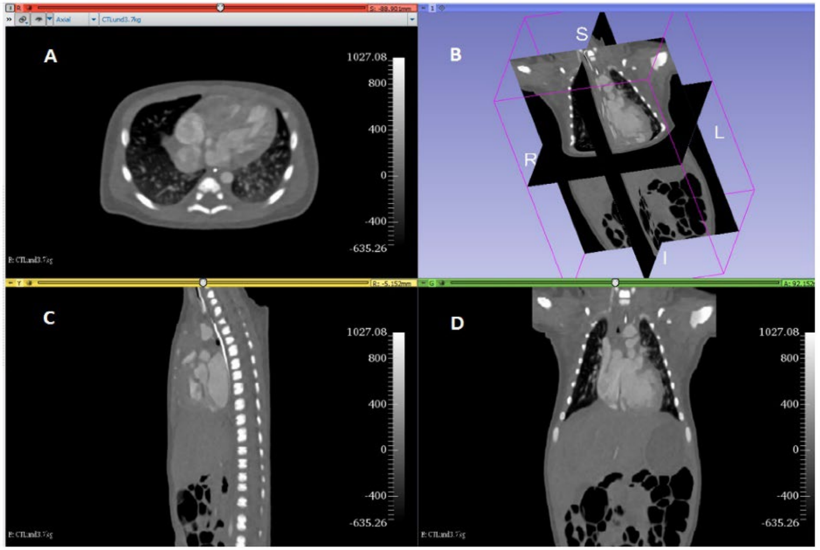
Assessment of open-field fluorescence guided surgery systems: implementing a standardized method for characterization and comparison

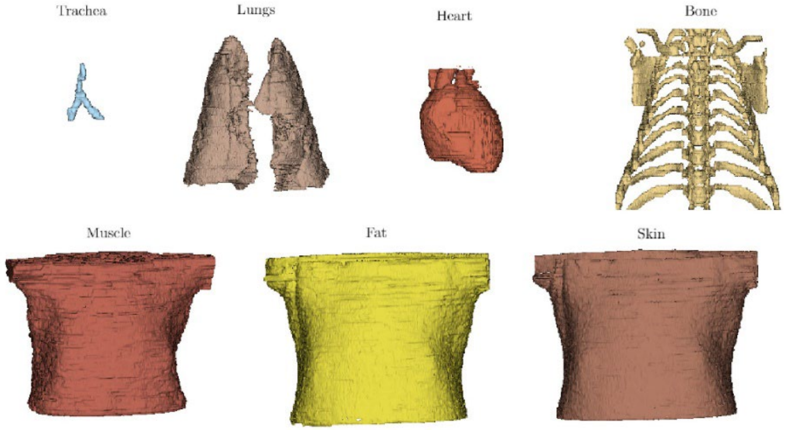
Marien I. Ochoa,[a] Alberto Ruiz,[b] Ethan LaRochelle,[b] Matthew Reed,[a] Eren Berber,[c] George Poultsides,[d] and Brian W. Pogue[a,*]

[a]University of Wisconsin Madison, Department of Medical Physics, Madison, Wisconsin, United States
[b]QUEL Imaging, White River Junction, Vermont, United States
[c]Cleveland Clinic - Marymount Hospital, Garfield Heights, Ohio, United States
[d]Stanford Medicine, Department of Surgery, Stanford, California, United States

doi.org/kzvf

Anthropomorphic Neonate phantoms



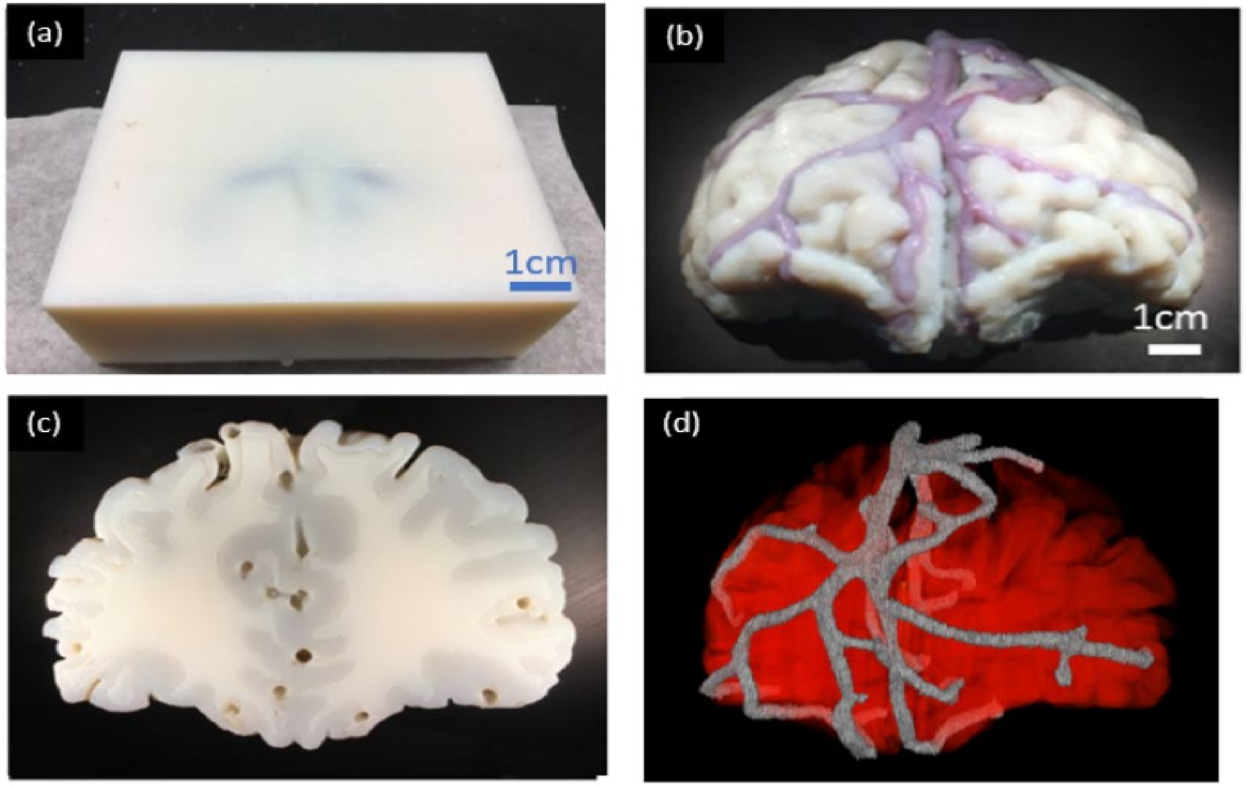


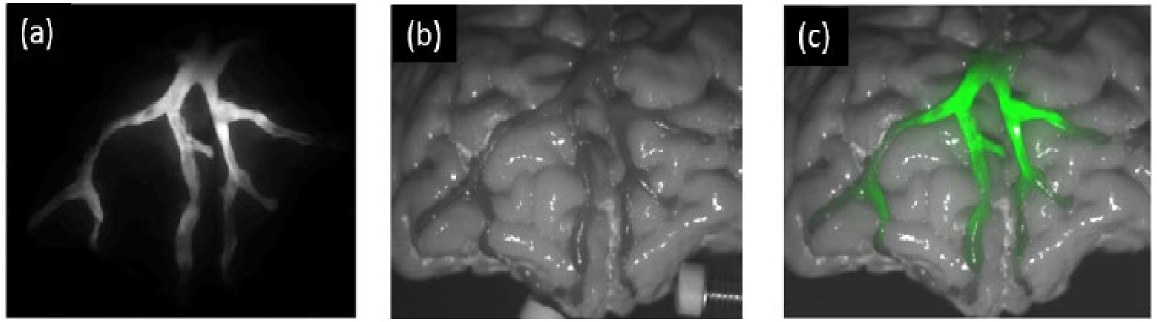
Biomedical Optics Express Vol. 10, Issue 4, pp. 2090-2100 (2019) • https://doi.org/10.1364/BOE.10.002090

Solid phantom recipe for diffuse optics in biophotonics applications: a step towards anatomically correct 3D tissue phantoms

Sanathana Konugolu Venkata Sekar, Andrea Pacheco, Pierluigi Martella, Haiyang Li, Pranav Lanka, Antonio Pifferi, and Stefan Andersson-Engels

3D Printed Phantoms & Targets





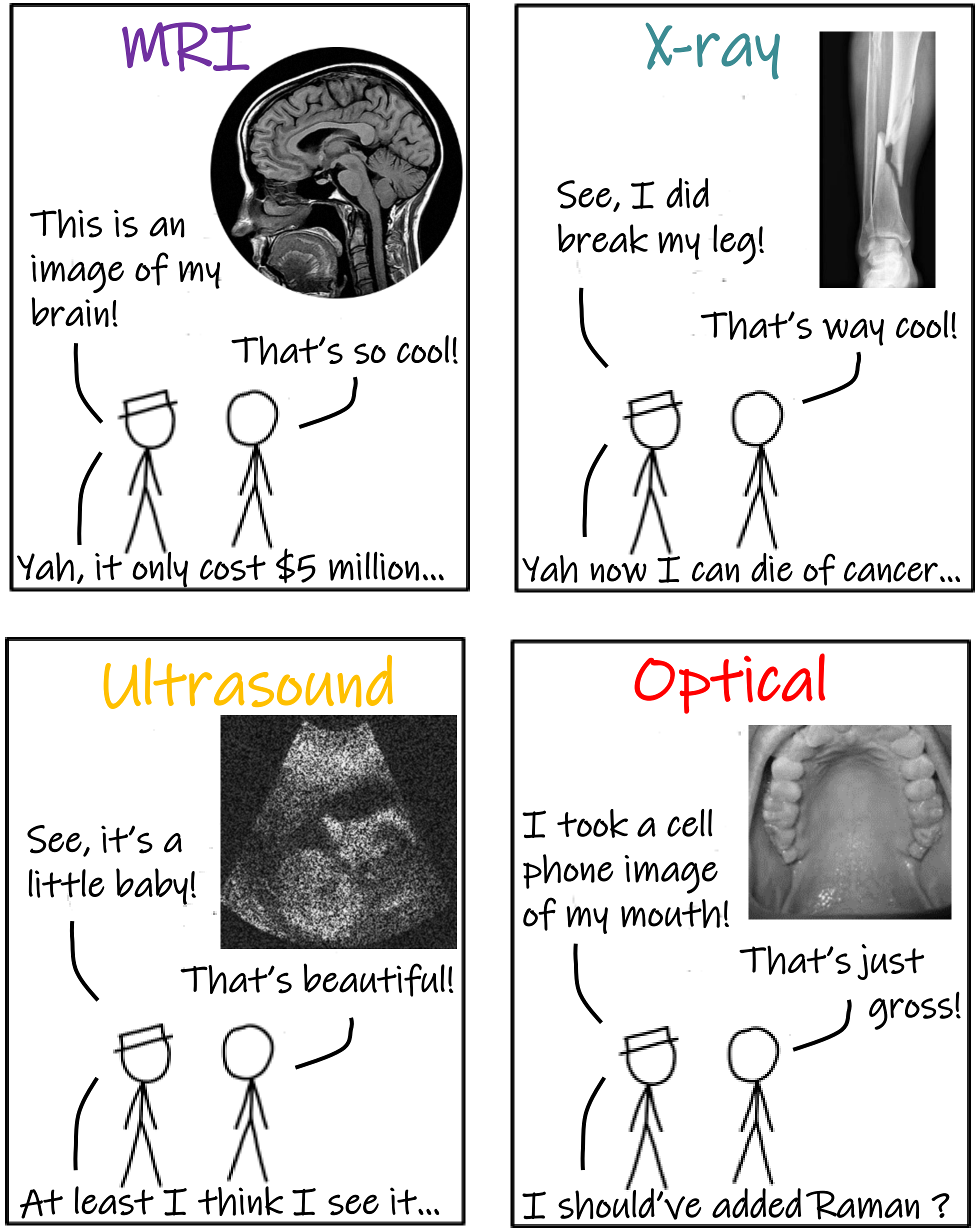
Liu, Y., et al. Biomed Opt Express, **9**(6): p. 2810-2824. (2018)
Wang, J.T., e*t al.* Proc of SPIE, **9325**. (2015).

Summary

- '***chicken or cheese***' are not useful for publication…
- **Low cost ≠ best - but it is both *'Art & Science'***
- Currently **voluntary** & largely **scientifically driven**
- **Phantoms & systems** should be developed in parallel
- **Each modality develops best practice** (OCT, PA, DOT, Surgery, etc)

- **Resin/Silicone based** have been optimal for stability & repeatability
- **3D printed** gaining wide adoption

- **Intralipid or Gel/Agar based for biological/chemical** compatibility


MRI
This is an image of my brain!
That's so cool!
Yah, it only cost $5 million...
X-ray
See, I did break my leg!
That's way cool!
Yah now I can die of cancer...
Ultrasound
See, it's a little baby!
That's beautiful!
At least I think I see it...
Optical
I took a cell phone image of my mouth!
That's just gross!
I should've added Raman ?

XKCD-like