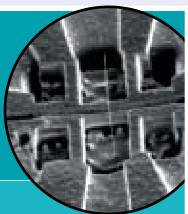
NPL
National Physical Laboratory

Health *Matters*

A National Measurement Newsletter
Winter 2008: **Issue 5**

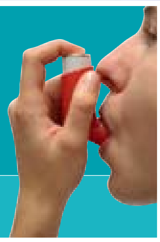
New standard for protein structure measurement

New calibration service for airborne nanoparticle number concentration



Page 3

Every breath you take



Pages 4 & 5

Modular laser safety training scheme for hospitals

Page 6

Department for **Innovation, Universities** & **Skills**

New standard for protein structure measurement

NPL, in collaboration with the University of Warwick, has developed a new reference material to improve the interlaboratory comparability of protein structure measurements by circular dichroism (CD). The material has been evaluated in an inter-laboratory study with Warwick, Chiralabs and NIBSC.

Proteins are an increasingly important class of drugs (they are known as biopharmaceuticals). Examples of biopharmaceuticals include Herceptin and Erythropoietin (EPO). The 3D structure of protein molecules determines their efficacy and safety; circular dichroism (CD) is one of the best approaches for measuring this. Consequently CD has become an important Quality Control tool for the biopharmaceutical industry, so it is important to obtain accurate and consistent CD measurements throughout the lifetime of an instrument, and for measurements to be consistent between different laboratories.

However, previous work by NPL has identified significant problems that occur when the results obtained from different laboratories are compared.

The new material, $Na[Co(EDDS)]\cdot H_2O$ (EDDS = N,N-ethylenediaminedisuccinic acid), has many advantages over the materials currently in use, including greater stability, and NPL is working towards making it commercially available. The interlaboratory comparison of this material demonstrated that it could improve CD comparability between laboratories, when compared to the standard materials currently used - camphor sulfonic acid and ammonium camphor sulfonate.

The CD spectrum of this new material has nine distinct peaks at wavelengths between 180 and 599 nm. In comparison ammonium camphor sulfonate, used as a secondary standard compound, only has one fully characterized CD band.

Another advantage is that the new reference material is readily available in both enantiomeric (mirror image) forms while camphor sulfonic acid - which is used as the current primary standard - is only readily available in one enantiomeric form. This new material therefore fulfils the principal requirements of CD calibration.

For further information, please contact:

Alex Knight

T: 020 8943 6308

alex.knight@npl.co.uk

This work, has been published in *Chirality* 20 (9), 1029-1038, A new reference material for UV-visible circular dichroism spectroscopy, and is available here:

www3.interscience.wiley.com/journal/119427816/abstract

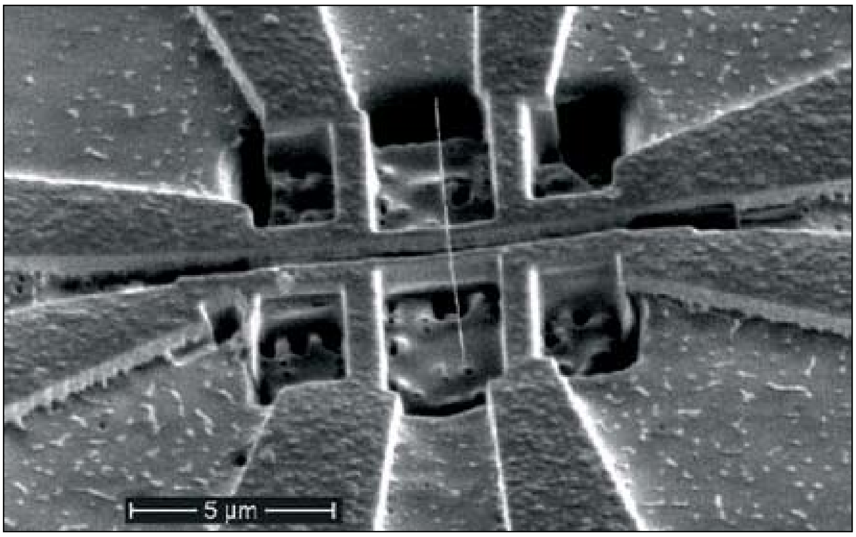
NPL's new calibration service for airborne nanoparticle number concentration

Concern about the impact of nanotechnology on our health has emphasised the need to monitor our exposure to engineered nanoparticles. NPL has now joined collaborative projects investigating the toxicological effects of nanoparticles, and has developed a calibration service for instruments that measure airborne nanoparticle number concentration.

Nanoparticles are particles or tubes whose smallest dimension has a scale of 100 nm or less, some of which are deliberately created for a variety of industrial applications, including cerium oxide and zinc oxide particles, and carbon nanotubes. These particles can become airborne, at which point they can be breathed in - an important exposure route.

There are many technical challenges to measuring the number of engineered nanoparticles found in a sample of air; importantly, normal outdoor air typically contains thousands of nanoparticles per cubic centimetre from non-engineered sources, mainly from vehicle exhausts and other types of combustion. Devising practical and reliable exposure measurement methods for particle number concentration and size distribution, and also methods to characterise other relevant properties of nanoparticles such as their surface area, are vital for the proper evaluation of the epidemiological and toxicological effects of nanoparticles.

With broad capabilities in physical and chemical measurement and extensive experience in field measurements of airborne particles, NPL is well placed to respond to these issues. This includes measurements of mass based measures like PM10 (Particulate Matter of <10 μm) and PM2.5 (Particulate Matter of <2.5 μm), as well as running Defra's Air Quality Network for Particles, which includes number concentration, size distribution, and chemical analysis.



A carbon nanotube bridge (vertical line, centre)

NPL is involved in collaborative projects investigating the toxicological effects of nanoparticles, and is leading efforts to bring these types of measurements into the metrological arena through organisations including EURAMET (the European Association of National Metrology Institutes) and ISO (the International Organization for Standardization). NPL has recently developed a calibration service for instruments that measure airborne nanoparticle number concentration, such as Condensation Particle Counters, and the service procedure has now been ISO 17025 (UKAS) assessed.

For further technical information please contact:

Paul Quincey

T: 020 8943 6788

paul.quincey@npl.co.uk

For further information on the instrument calibration services available in the area of Environmental Measurement, please visit:

www.npl.co.uk/environment/inst_calib.html

Every breath you take

A new breath monitoring technology can be evaluated and fine-tuned for several applications, including asthma monitoring, thanks to a new test facility designed with the help of NPL.

An innovative breath monitoring device for several medical applications has been developed by Anaxsys Technology, which specialises in respiratory measurement. When Anaxsys needed to create a test facility for their instruments they sought advice from NPL's specialists in the generation of precision gas mixtures.

Breath monitoring is central to the diagnosis and care of asthma, emphysema, and other respiratory conditions. But many breath monitoring devices require the user to exhale forcefully, or to deliver a full lungful of air. This can be impossible for patients who are seriously ill, or unconscious, and for infants.

There is a clear need for more flexible and user-friendly monitors. To address this, Anaxsys have developed a technology platform consisting of a variety of new sensors. Rapid response times follow transients within individual breaths, allowing valuable data to be captured during normal breathing.

In the early stages of development, sensor testing depended heavily on volunteers from the Anaxsys research team. NPL helped Anaxsys clarify their testing and calibration needs for both development and production. Anaxsys visited NPL to understand how standard gas mixtures and defined humidities are generated. A design review by NPL enabled Anaxsys to improve their design, and construct a test facility.

Quantitative testing is now enabling Anaxsys to characterise and tailor certain sensors, so that the objective parameters of the sensors can be correlated with medical outcomes in clinical tests. As a consequence, the sensors can now be refined for different applications, possibly to include respiratory rate monitoring after operations, and even early screening for lung cancer – in addition to the main target area of asthma care.

'Many breath monitoring devices require the user to exhale forcefully, or to deliver a full lungful of air. This can be impossible for patients who are seriously ill, or unconscious, and for infants.'

Image courtesy: Anaxsys Technology

For further information, please contact:
Stephanie Bell
T: 020 8943 6402
stephanie.bell@npl.co.uk

NPL specialises in certifying a wide range of gas species and amount fractions with guaranteed uncertainties to meet specific customer requirements. For further information and the enquiry form, please visit:
www.npl.co.uk/analytical/gas_mix.html

Modular laser safety training scheme for hospitals

NPL, in partnership with SEEDA (South East England Development Agency) and Southampton General Hospital, has developed and run a pilot course for hospital laser safety advisers (LSAs) entitled "Optical Radiation Safety in the Clinical Environment". Piloted on 7 August 2008 at Southampton General Hospital, the aim of the training is to address the optical radiation safety training needs of the healthcare sector, and to prepare businesses and employees for the impact of the new Artificial Optical Radiation Directive (AORD).

One of the key objectives of this project is to prepare businesses and employees in the SEEDA region for the incoming Artificial Optical Radiation Directive (AORD) through structured training. The new directive introduces provisions on risk assessment, control of exposure, health surveillance and information, instruction and training, and will be implemented into UK law in April 2010 by the Health and Safety executive.

Medical professionals operate in environments in which multiple optical sources including laser scalpels, theatre lights and diagnostic sources such as optical coherence tomography produce optical radiation of varying degrees. This can be harmful if individuals are subjected to too much radiation or handle equipment inappropriately.

In 2007 NPL won a grant under the SEEDA Training Pools program to develop a new NPL Training Framework in the areas of clinical thermometry and optical radiation technologies, working with partners to launch the training courses in the SEEDA region. A pilot focusing on optical radiation safety has been carried out successfully.

All attendees were complementary regarding the balance between theory and practical elements as well as the networking opportunities created during the day.

Nine LSAs from widely dispersed NHS trusts within the SEEDA region were provided with the latest guidance for optical safety and standards and mentored through comprehensive risk assessment case studies in small groups. The presentation and documentation were both rated "excellent" by all the course attendees.

The purpose of the NPL training framework is to raise the quality of measurement throughout organisations. It has already been successfully applied to Dimensional Metrology, where training is now available to measurement users. The modular structure of the course is designed to make it flexible enough to fit around the schedules of individuals, and to allow course structures to be tailored to businesses and qualification bodies that have differing training requirements.

The training programmes for optical radiation safety and risk assessments were both rated excellent by registrees, who especially appreciated the flexibility of the framework. All supported the development of this pilot course into a full programme - requesting that similar courses be provided in future.

NPL will be running this course from 2009, if you would like to register your interest please e-mail:

Tom Ashby
tom.ashby@npl.co.uk

For technical information, please contact:

Simon Hall
T: 020 8943 6758
simon.hall@npl.co.uk

NPL participates in infrared ear thermometer calibration project

Infrared ear thermometers (IRETs) are commonly used in hospitals, but there are concerns over their accuracy and performance. NPL has taken part in an international comparison to assess the calibration sources (blackbodies) used to provide traceable calibrations of IRETs.

NPL has completed its measurements for EURAMET project 927 – 'Comparison of blackbodies for calibration of infrared ear thermometers'. This is a comparison project involving ten countries, coordinated by the University of Ljubljana, Slovenia. Its purpose is to compare capability for the calibration of infrared ear thermometers (IRETs).

IRETs are widely used in hospitals and medical practices, but there is some concern over their accuracy and performance compared to using more traditional instruments such as mercury-in-glass thermometers. Although some issues are due to their use within the medical environment, a key issue is their calibration accuracy. Measurements carried out at NPL have indicated that some of the lower cost devices can have a significant calibration offset and can drift substantially over periods of minutes. It is therefore essential that the calibration and performance of IRETs are verified using a high quality, traceable blackbody calibration source.

The project compares each laboratory's blackbody calibration with a transfer blackbody source that is currently being circulated amongst the participants. The comparison is carried out at different temperatures over the operational range of the IRETs, using both the circulated transfer IRET, as well as the laboratory's own IRET (where possible).

NPL has traditionally been very involved in calibration and international standardisation issues associated with IRETs. This has included contributing towards a new ISO document for electrical clinical thermometers (which incorporates IRETs) as well as other international comparison projects, including one with PTB, Germany and NMIJ, Japan. Participation in EURAMET project 927 has enabled NPL to maintain and strengthen this involvement.

For further information, please contact:

Helen McEvoy

T: 020 8943 6183

helen.mcevoy@npl.co.uk

Point-of-care devices

Lateral flow devices are instruments used to monitor a patient's condition at the point-of-care, rather than sending samples away to be tested in laboratories. NPL are currently designing an imaging system that will aid in the development of calibration procedures for lateral flow devices. NPL hopes to identify common weaknesses in measurements taken on lateral flow devices.

Lateral flow devices are point-of-care (POC) tests that can be used in the diagnosis of diseases or other conditions, or during the mitigation, treatment, or prevention of diseases, in humans and animals. Well-known examples of POC tests include blood glucose and home pregnancy tests, which are activated upon the addition of a biological sample. Other less familiar POC tests applications include tests for drugs of abuse, heart attack, HIV, malaria and respiratory diseases.

Lateral flow tests are designed to detect the presence of a target molecule in a sample using antibodies. A typical test strip consists of chemical reagents deposited on microporous membranes that are laminated onto a semi-rigid plastic backing material. These membranes are then placed inside a plastic enclosure. Upon applying the sample, e.g. blood or urine, to the test strip, the molecule of interest binds to an antibody that is complexed to a coloured nanoparticle (often red or blue) and flows along the membrane where it encounters a second antibody molecule. At this point the molecule of interest, which is attached to the coloured reagent, is concentrated to form a coloured line.

Important considerations when designing POC devices include the need for the tests to be easy enough for non-specialists to use, these need to be robust and reliable, and they must meet pre- and post-market regulation control. As well as providing a positive or negative response (qualitative test), the colour intensity of the test line can be measured using test-strip readers to give quantitative information. Such quantitative measurements, if digitally read, not only reduce ambiguity in the interpretation of the coloured line, but can also help optimise test designs and manufacturing processes, and verify that the system acts in an accurate and repeatable manner.

'Important considerations when designing POC devices include the need for the tests to be easy enough for non-specialists to use.'

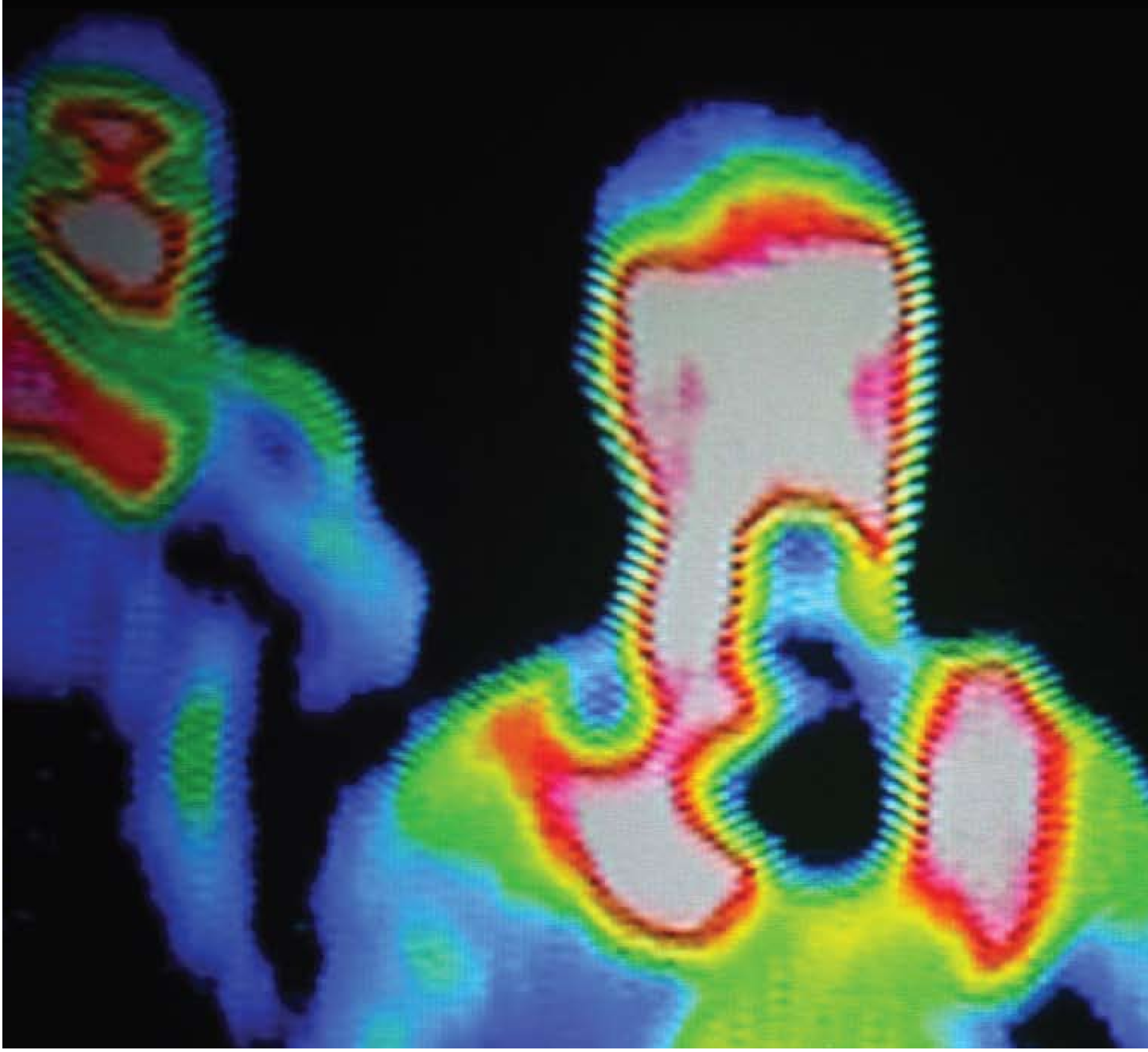
NPL is now designing an imaging system using charge-coupled device (CCD) technology to develop calibration procedures for lateral flow devices using biological samples. The work will seek to identify common weaknesses in measurement practice that give rise to inaccurate diagnoses, including the effect of interfering substances. NPL also aims to develop a method for establishing a line of traceability from clinical laboratory derived results to a POC device. A line of traceability between enzyme-linked immunosorbent assays (ELISA) and lateral flow devices will also be developed. The overall aim involves designing a digital calibration system, which can be used in any clinical laboratory for use with lateral flow strips prepared by a range of manufacturers. This will enable test reliability, remove operator dependence and enable comparison across different testing environments to provide improved point-of-care testing for patients.

For further information, please contact:
Smita Thobhani
T: 020 8943 6684
smita.thobhani@npl.co.uk


0:00 0:00
5.7
mmol/L
M
S

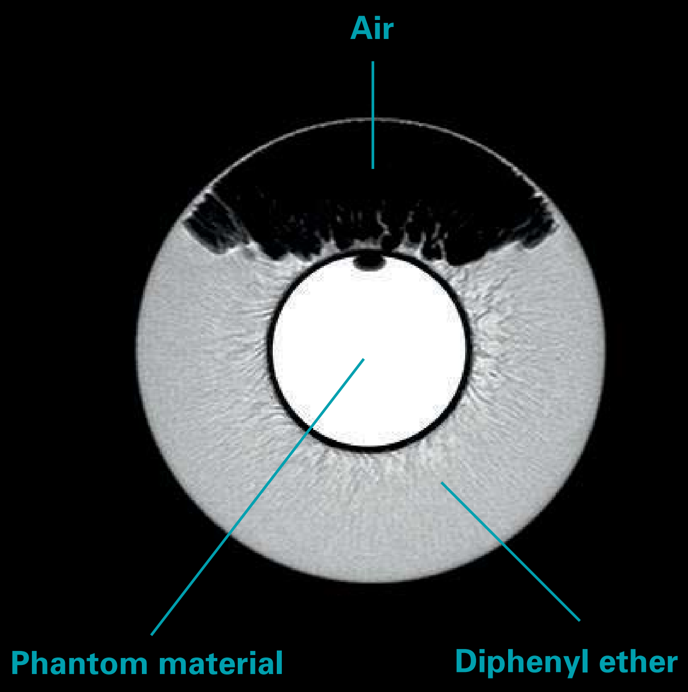
Calibration of MRI thermometry using temperature reference targets based on organic fixed points

Magnetic Resonance Imaging (MRI) thermometry can be used to map temperatures throughout the body, helping to apply thermal medical therapies correctly. To calibrate the system and overcome the problem of drifting, NPL has developed novel organic fixed-point targets for MRI thermometry.



MRI thermometry provides a unique way of mapping temperature within the human body. Such a map can provide useful information for thermal based medical therapies such as laser, RF, ultrasound and hypo/hyperthermia, enabling close treatment control and monitoring. However, MRI thermometry can suffer from drift, causing uncertainty in the absolute temperature.

NPL has conceived and developed novel organic fixed-point targets for MRI thermometry. These targets provide a stable reference source of accurately known temperature for validation and calibration. The targets were developed at the temperatures of 26.3 °C and 35.8 °C, based on the freezing of the organic fixed points: diphenyl ether and ethylene carbonate.



MRI image of the diphenyl ether reference target. The target comprises two concentric glass spheres: the inner sphere contains phantom material for investigating MRI thermometry. The outer contains the organic fixed point material undergoing freezing that maintains a fixed temperature to within 0.1 °C for at least 2 hours

NPL has collaborated with Manchester University to perform magnetic resonance spectroscopic (MRS) thermometry measurements of the targets, using an MRI scanner at the Wellcome Trust Clinical Research Facility, Manchester University.

A reference target for calibrating MRI thermometry

Phantom material for MRS thermometry is a material that has a similar nuclear magnetic resonance (NMR) spectroscopic signature to brain tissue. The phantom material used contains N-acetyl aspartate (NAA) and water, both found in the brain. In MRS thermometry, an NMR spectrum is recorded for a voxel (typically 15x15x15 mm) from which the proton chemical shifts of water (δ_{H2O}) and NAA (δ_{NAA}) are measured. Temperature is determined by exploiting the linear temperature dependence of δ_{H2O} relative to δ_{NAA}.

It is notable that the original calibration for MRS thermometry does not agree with the reference target measurements. This will be partly due to the nature of the phantom material (its ionic strength, metal ions and protein content), which differs from that used in the original calibration. In future work we will investigate systematically the effects of composition on the measured temperature, and the improved calibration achieved by NPL will play a part in this. With the use of reference temperature standards within the bore of the MR magnet, NPL aims to enable a more accurate temperature calibration curve to be generated for in vivo studies.

For further information, please contact:

Andrew Levick

T: 020 8943 6301

andrew.levick@npl.co.uk

Call for Papers

Radiotherapy Dosimetry: Current Status and Future Developments

26 February 2009, NPL, Teddington

One day meeting to review the current state of clinical radiotherapy dosimetry, and learn about recent developments in the field. NPL will be providing the venue for this meeting.

Presentations are invited on all aspects of radiotherapy dosimetry, including: IMRT, IMAT, Tomotherapy, radionuclide, brachytherapy, 3D, in vivo and small-field dosimetry.

Proffered speakers will have free registration for the meeting.

For programme information please visit:

www.bir.org.uk

The deadline for submission of abstracts is Friday 5 December 2008. Abstracts should be e-mailed to:

Dr John Mclellan

T: 020 7307 1411

john.mclellan@nhs.net

Forthcoming Events:

Radiotherapy Standards Users' Group

1 December 2008

NPL, Teddington

The Radiotherapy Standards Users' Group meets at NPL about every eighteen months, attended by around fifty radiotherapy physicists from throughout the UK and Ireland.

www.npl.co.uk/rsug
clare.gouldstone@npl.co.uk

Wheatstone Lecture 2008 - Time by wire: 175 years of the Greenwich Time Service

3 December 2008

The IET, Savoy Place, London

In this illustrated, lively and thought-provoking lecture, the Royal Observatory's curator of timekeeping will explore the curious history of time distribution from Greenwich, revealing little-known stories behind one of Britain's best-known measurement systems — Greenwich Mean Time

www.theiet.org/events/2008/wheatstone.cfm

High Accuracy Freeform Measurement of Optical & Orthopaedic Surfaces

29 January 2009

Loughborough University, Leicestershire

This EMAN meeting will present and discuss a range of measurement and characterisation techniques that can be applied to optical and orthopaedic freeform surfaces.

www.npl.co.uk/events/090129_highacc.html
hannah.carter@npl.co.uk

What is the National Physical Laboratory?

The National Physical Laboratory (NPL) is one of the UK's leading science facilities and research centres. It is a world-leading centre of excellence in developing and applying the most accurate standards, science and technology available.

NPL occupies a unique position as the UK's National Measurement Institute and sits at the intersection between scientific discovery and real world application. Its expertise and original research have underpinned quality of life, innovation and competitiveness for UK citizens and business for more than a century.

www.npl.co.uk

Health*Matters*

If you would like further information on any aspect of **Health***Matters*, please contact:

Daniel Ainsworth
Health*Matters* **Editor**
National Physical Laboratory
Teddington
Middlesex
UK TW11 0LW

Helpline: 020 8943 6880
Fax: 020 8614 0446
E-mail: **enquiry@npl.co.uk**

7841/SEA/2k/1108