NPL
National Physical Laboratory

Health *Matters*

A National Measurement Newsletter

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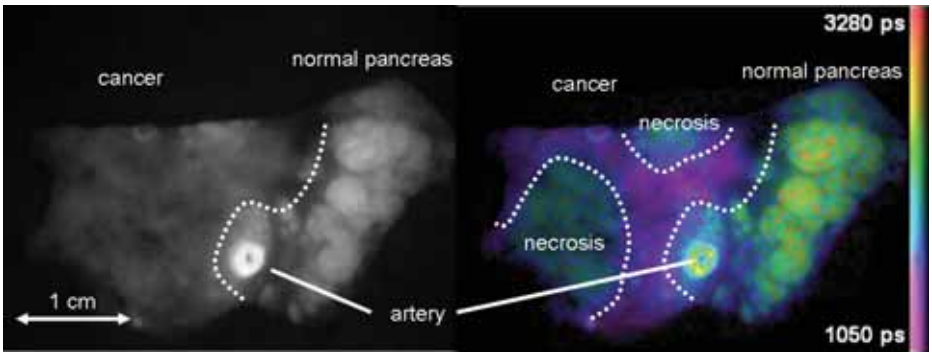

Courtesy of Neil Gallety and James McGinty, Imperial College, London

FLIM detection of pancreatic cancer

Imaging the nanoworld

Fluorescence lifetime imaging microscopy (FLIM) is fast becoming the imaging and analysis tool of biological systems, nanotechnology and microfluidics. NPL has developed methods of validating these techniques.

FLIM allows the lifetimes of one or more light emitting species to be spatially resolved and can be used to provide information about the state of the fluorescent species and their immediate molecular environment.

The fluorescence lifetime is sensitive to environmental conditions such as pH, and excited state reactions such as fluorescence resonance energy transfer (FRET) or collisional quenching. Such properties are key for resolving physiological parameters in the cell.

However, the calibration, determination of resolvable lifetime differences and evaluation of artefacts have not been extensively treated. NPL's Optical Radiation Measurement (ORM) team has conducted measurements on important molecular probes, including quantum dots and enhanced green fluorescent proteins (EGFP) and the development of mathematical modelling techniques.

Using NPL's techniques, it is now possible to make traceable measurements of candidate fluorescence lifetime standards. These new methodologies are vital to validate measurement systems in the fields of drug discovery, clinical diagnostics and biomedical imaging.

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Inside:

Quick facts

- Quantum dots are nanocrystals, measuring 2 to10 nanometers, which have fluorescent properties when stimulated by UV light.
- Quantum dots can be used as unique bio-labels that bind simultaneously to specific DNA sequences. Using fluorescence spectroscopy such as FLIM, tumours can be distinguished from normal healthy cells.

dti
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Developing standards for tissue engineering

NPL is working with other international measurement institutions to develop and conduct comparative studies to support the tissue engineering field.

Even from a cursory glance through the tissue engineering literature, it is apparent that there are currently no common procedures in place for assessing, for example, the viability of cells growing in a tissue scaffold or the consistency of some of the scaffolding materials such as alginates and collagens. This poses a fundamental issue for researchers, regulators and for commercialisation: how can you be sure that what you are doing is reproducible? The answer to this question may, at least in part, lie in the development of standards.

Standard documents outline globally accepted methods for evaluating materials, assessing structures, monitoring tissue development and appraising the 'quality' of the final product. In principle, this is a straightforward task, but unfortunately, this is not true for tissue engineered medical products. Many of the existing standards and those that are being developed take the form of Guides and come from ASTM International, an international voluntary standards development organization. An ASTM Guide is an informative document that describes several solutions to solving a measurement problem, discussing the pros and cons of each. Guides are produced when there is no simple solution to solving a measurement problem. Translation of these Guides into 'traditional' standards will take time and require a number of international round robins to identify the 'best' procedures.

A newly formed international committee operating under the VAMAS envelope has taken on the task of organising these round robins. The committee has strong links with standards bodies including ISO, DIN and ASTM and consists of representatives from national standards laboratories, academics and industry. The committee which includes NPL, has identified three initial project areas:

- The interpretation of tissue scaffold images
- Measurement of cell adhesion in a laminar flow cell
- Assessment of a hydroxyapatite/ collagen matrix

Details of the round robin are currently being developed and a call for participants will be issued shortly. If you would like further details about the committee, its goals or would like to be involved in the round robins then please contact:

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www.astm.org
www.vamas.org

Coherent health

Optical Coherence Tomography (OCT) is a non-invasive technique for looking at the internal structure of biological tissue. NPL is working with industrial and academic partners to develop a better understanding of OCT and exploit new applications.

In the eye

When OCT is used to measure the human eye, the results are given in optical path lengths. If the refractive index of the sample is known then the geometric distance can be calculated. NPL is leading the development of an algorithm to separate the refractive index and the geometric depth. This may enable OCT to be used as a diagnostic tool to detect diseased tissue, and potentially as a replacement for biopsies.

Tissue scaffolds

NPL is using OCT to investigate the properties of tissue scaffolds. These are structures that are seeded with cells and used as a frame upon which to grow tissue formations, such as arterial tissue for vascular grafts. They are also used to distribute the nutrients that cells need to grow. NPL is using OCT to examine the complex fluid dynamics around the pores of the scaffold, and to measure the flow of cells and nutrients. Scientists are also creating images of the changes and deterioration in a scaffold while it is replaced by tissue as cells grow. This affects the movement of nutrients. Knowing how the wall thickness changes, and how this affects the structural and material properties, can ensure the most efficient design of new scaffolds.

Get your teeth into this

OCT is also being examined as a potential tool for imaging teeth and dental compounds to monitor the health of teeth, the effectiveness of dental treatments and the curing of the compounds themselves. Having a better understanding of the internal structures of the teeth after treatment should lead to more effective treatments and less time spent in the dentist's chair!

NPL has launched an OCT interest group. For further information contact Pete Tomlins
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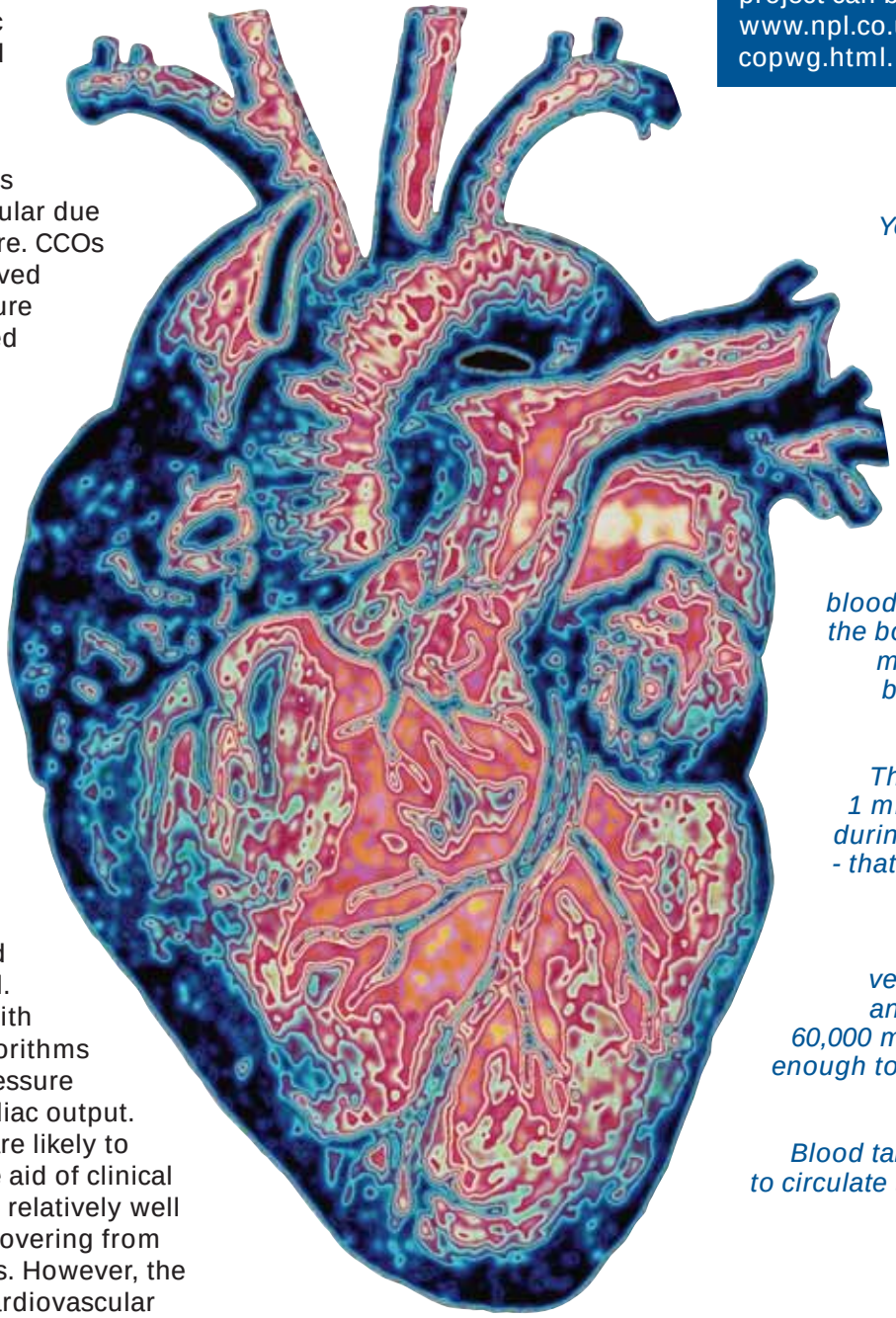
A hearty measure

NPL has teamed up with Guy's & St Thomas' Hospital and Cranfield University in an effort to improve the traceability of Continuous Cardiac Output (CCO) measurements.

CCO measurements determine the volume of blood being pumped by the heart in litres per minute. These measurements provide a vital tool for the diagnosis and treatment of the critically ill and for monitoring patients recovering from surgical procedures. Historically, cardiac outputs are derived from catheters inserted into the pulmonary artery but this technique is becoming less popular due to its invasive nature. CCOs are now being derived from arterial pressure waveforms obtained from catheters inserted into the radial and/or femoral arteries.

Clinicians need confidence that the measured CCO values are correct and, whilst the current generation of CCO instruments are capable of providing real-time monitoring of patient conditions, errors may arise when they are used with the critically ill. The problem lies with the proprietary algorithms that convert the pressure waveform to a cardiac output. These algorithms are likely to be derived with the aid of clinical data obtained from relatively well patients - those recovering from surgical procedures. However, the behaviour of the cardiovascular systems for critically ill patients can quickly depart from the norm, and therefore the CCO values predicted under these circumstances may be incorrect and lead to a faulty diagnosis and hence non-optimal treatment.

This NPL joint research aims to develop a device for generating traceable pressure waveforms and to improve the cardiovascular model used to predict the cardiac output.



As part of the DTI's NMS Engineering Measurement Programme 2005-2008, a Centre for Dynamic Measurement is being established at NPL.

The aim of the Centre is to act as a focal point for research and advice on measurement made under dynamic conditions.

Details of this new project can be found at www.npl.co.uk/dynamic/copwg.html.

Your heart beats about 100,000 times in one day and about 35 million times in a year. During an average lifetime, the human heart will beat more than 2.5 billion times.

Your body has about 5.6 litres of blood. It circulates through the body three times every minute. In one day, the blood travels a total of 12,000 miles.

The heart pumps about 1 million barrels of blood during an average lifetime - that's enough to fill more than 3 super tankers.

Your system of blood vessels – arteries, veins and capillaries – is over 60,000 miles long. That's long enough to go around the world more than twice!

Blood takes about 20 seconds to circulate throughout the entire vascular system.

For further details on NPL's research in CCO measurements please contact:
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Courtesy of Science Photo Library

Bundling services to hospitals in a new type of contract

To facilitate budgeting, many hospitals are now negotiating multi-year contracts with NPL, incorporating calibrations and other services.

These contracts known as SLAs (service level agreements) were introduced earlier this year to soften the blow of the price rises that became necessary because of the ending of the substantial DTI subsidy for radiotherapy, nuclear medicine and diagnostic radiology services. The SLAs will spread the costs evenly over the period, with single annual payments. However, they have been extended to cover other services to hospitals, including ultrasound, audiometry, UV dosimetry, surface contamination, tympanic thermometers, plus radiotherapy training and audit services.

This new concept was first suggested at an Open Forum for senior medical physicists held at NPL on 13 March 2006 to discuss the implications of the withdrawal of the DTI subsidy. The radiotherapy community was updated on progress by a presentation and exhibition stand at the IPEM Biennial Radiotherapy Meeting in Norwich on 3-4 July 2006. The key documents and presentations from these two meetings are available for download from

www.npl.co.uk/ionrad/services/health

In particular, on this webpage there are questionnaires (in Word and pdf) to be completed by those seeking to enquire about an SLA contract to meet their particular needs.

In order to keep costs down, following the loss of DTI subsidy, the radiotherapy and diagnostic radiology services have undergone thorough review and revision. As a result, from 2007 onwards, there will be only one calibration period per year for the therapy level photon, electron and electrometer services, and this will be in the spring each year.

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Improved clinical diagnosis and therapy

Brain damage in thousands of babies may be prevented thanks to a collaboration between NPL and hospital trusts.

Segmented EC cell MRI images post initiation

They will be working together to develop magnetic resonance imaging (MRI) to measure the core temperature of the human brain. The risk of brain damage in babies deprived of oxygen is reduced if the brain is cooled during the first 48 hours.

The project is the first of its kind, with NPL scientists working closely with MRI experts at three UK hospitals, University College Hospital, Hammersmith Hospital and Royal Marsden Hospital, who are providing valuable technical expertise and are making the expensive MRI scanners available.

MRI is used by a number of research groups to map the temperature field of human tissue or food. However, MRI thermometry has not been calibrated to establish traceabilty to the International Temperature Scale (ITS-90). NPL's role is to develop a 'phantom target' of accurately known temperature to validate and calibrate MRI scanners used to measure the temperature. The 'phantom target' will comprise of a sphere of material that simulates the properties of human tissue surrounded by "organic fixed point" material that holds the tissue at a known stable temperature. When placed inside the MRI scanner it provides a temperature calibration point for MRI thermometer.

Progress to date includes:

- Literature survey of recent developments in MRI thermometry and several groups were identified for possible collaboration.
- MRI images taken of one of our ethylene carbonate fixed-point cells during freezing. The scans clearly show the solid and liquid phases.
- Drawn up designs for the spherical target.
- Calibration and drift measurements of our fluoroptic thermometers. These are suitable for use in the radiofrequency field of MRI scanners.

MRI uses radio-frequency detection in high magnetic fields, with no exposure to damaging forms of radiation. It is primarily used to provide clear diagnostic images, but it can also map temperature, blood-flow and chemical composition.

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A new dosimetry service for advanced radiotherapy

NPL have launched a new service to provide the only traceable measurements of dose for TomoTherapy machines.

Simon Duane of NPL and Milan Tomsej from VUB Hospital setting up to make measurements in a TomoTherapy machine.

This service will be used during commissioning and for other quality assurance checks of TomoTherapy machines. TomoTherapy machines are a cross between a CT scanner and a conventional clinical linear accelerator. Based on previous pioneering work in NPL's Radiation Dosimetry team, the sensitivity of alanine dosimeters were increased to the point where they can be used to measure the doses typically delivered to cancer patients in radiotherapy. This technology has recently been adapted to the particular requirements of helical tomotherapy, a new and highly integrated technique to deliver Intensity Modulated Radiation Therapy (IMRT), which is now in routine use at the Cromwell hospital, London. The Cromwell Hospital is the first hospital in the UK to get a TomoTherapy machine. NPL staff carried out measurements at the Cromwell Hospital and the results reported before the first patient treatment in May.

In response to requests for similar calibration of their machines by other TomoTherapy users, a mail-order version of the service was successfully tested in collaboration with medical physicists at the VUB hospital in Brussels in June. The new service is now available from NPL on a commercial basis, and RISO, the Radiotherapeutic Institute in Deventer, Netherlands, used it in August to calibrate two new TomoTherapy machines for treatment of their first patients.

The rapid development, from initial discussions with TomoTherapy Inc in August 2005, to an established calibration service operating on a commercial basis within 12 months, was only possible thanks to the rapid turnaround of work at key stages by NPL Engineering Services and chemical dosimetry staff in NPL's Radiation Dosimetry team. NPL plans to move on to use this same system to make measurements of dose in more conventional IMRT beams, as produced by clinical linear accelerators.

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Clinical Temperature Measurement and Thermography Meeting: Call for Papers

Organised by the IPEM's Physiological Measurement Group and co-sponsored by NPL's Thermal Measurement Awareness Network and the UK's Thermography Association, the Clinical Temperature Measurement and Thermography Meeting will be taking place on 2 – 3 May 2007 in Cardiff.

Over the last fifteen years new technologies have been developed to replace traditional mercury thermometers. A variety of temperature measuring devices have become popular in clinical use, using tissue contact (e.g. in the mouth, axilla, skin or rectum) or non-contact devices using infra-red sensing (designed for the ear or forehead). These changes raise a range of issues including the standardisation of calibration methods, clinical practice and clinical accuracy.

This meeting aims to address issues of instrument calibration, quality assurance, and future developments in medical thermometry and thermography.

For more information and abstract submission please contact:
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May I help you: Protecting call-centre workers

NPL is investigating the problem of acoustic shock; sudden sound bursts through headsets, a phenomenon of increasing concern for all UK call-centres.

Almost 900,000 people working in the UK call-centre industry are at risk of exposure to acoustic shock, with profound effects, including permanent ringing in the ears, various types of hearing difficulty and psychological symptoms. In the UK alone, this has led to over £2M in out-of-court settlements.

Acoustic shock can be caused by sounds which are much quieter than those guarded against by the Control of Noise at Work Regulations 2005. The mechanisms involved are yet very poorly understood, and NPL is working in partnership with the Acoustic Safety Programme (ASP) to investigate the subject and help alleviate the problem.

A test facility has been established with initial funding from the DTI and ASP to assess the performance of the various devices on the market that are designed to protect call-centre workers. Part of this facility is a device that simulates the human ear, built into a structure, which can 'wear' headsets and earphones (see image). If the ASP-NPL Research Partnership secures funding, the next phase of the project will take place in call-centres, and will aim to maximise the protection of workers, investigate shock signals, and provide expert medical assessment and assistance for people suffering from acoustic shock.

To learn more about Acoustic Shock and the Acoustic Safety Programme, please contact:
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www.acousticsafety.org

Absorbing research

NPL is helping the Heath Protection Agency to understand the effects of mobile phone radiation on human health.

There has been increasing debate about the effects of radiation from mobile phones, and the need to ensure they are safe for users. Effects under study include human cognitive speed, the release of stress proteins in nematode worms (indicating cell health), and excess calcium release from cells that can cause them to become cancerous or die.

The international safety standards for Specific Absorption Rate (SAR) of radiation into human tissue assume there is an impact on health from the heating effect of electromagnetic power. There is also a potential impact from non-thermal effects at levels below the limits set by the SAR standards.

The Mobile Telecommunication and Health Research programme (MTHR), made up of more than 30 UK research teams, investigates whether such effects actually occur. The research is sponsored by the DTI and Department of Health with joint funding from government and the mobile communications industry. Traceable metrology is at the heart of the MTHR studies. It is essential to know quantitatively what SAR doses are delivered in the research experiments – either to cells, worms or human volunteers.

Most research expertise in the MTHR programme is in medicine, biochemistry and physiology. The programme therefore needs to ensure its metrology is valid.

NPL advises the management committee and individual MTHR research teams on the design and use of exposure devices and SAR monitors. It provides advice on test rig design, measurement uncertainty, dummy phone exposure devices, and dielectric measurements.

NPL works with more than 15 research teams in MTHR to calibrate measurement equipment, supply and evaluate a screened room and supply other calibrated equipment.

While NPL advises on the metrology of mobile communications health research, the UK's Health Protection Agency (HPA) advises on health issues relating to electromagnetic radiation exposure.

For more information on NPL's mobile phone research contact:

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Further information on the MTHR Programme can be found at www.mthr.org.uk/

New Good Practice Guide for metrology in Nuclear Medicine

NPL has been working with representatives from the medical physicists' professional body (IPEM) to develop a new Good Practice Guide to reduce the risk to patients undergoing radionuclide therapy.

Nuclear medicine is a growing field, due largely to advances in biotechnology and imaging techniques such as Positron Emission Tomography. Some 670,000 patients are injected with radioactive compounds per year in the UK for diagnostic imaging or for therapy. Radioactivity is, of course, a known carcinogen, so for the safety of the patients it is important that the minimum quantity of radioactivity injected is compatible with obtaining a good quality image or effective treatment. To reduce the risk to the patients and for compliance with regulations, the radioactivity content (Bq) of each patient dose is checked in the hospital using an instrument called a 'Radionuclide Calibrator'.

The new guide (Good Practice Guide No. 93) *Protocol for Establishing and Maintaining the Calibration of Medical Radionuclide Calibrators and their Quality Control* will assist all the 250 UK hospitals involved in nuclear medicine on the use of Radionuclide Calibrators. Following the guide, hospitals will be able to demonstrate traceability to national standards at the required level of accuracy (better than +/- 5%).

The guide is available as a free download from the NPL publication website: www.npl.co.uk/publications/good_practice

Hard copies can be ordered for a fee through the NPL e-store:

www.npl.co.uk/e-store/

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Programme formulation update

The 2007 – 2010 DTI National Measurement System (NMS) combined programme for Acoustics and Ionising Radiation is now being formulated. One of five new core programmes, it will combine Acoustics and Ionising Radiation. This affiliation will have benefits in the healthcare, environment, and defence fields.

In May 2006, consultation meetings were held with relevant user communities to prioritise needs. The programme formulators are now defining the projects and are keen to identify projects that can be conducted collaboratively with partners who bring another source of funding to complement DTI funding. Much more can be achieved with combined resources and so please contact us if you wish to discuss possible ideas for collaboration.

Whether or not you participated in the user consultation phase, there is another opportunity to influence the content of the new programme. The DTI public consultation, expected to run from March to May 2007, will invite you to comment on the detailed programme document.

To keep in touch with this and other developments, please visit the formulation website at www.npl.co.uk/formulation

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Forthcoming events

www.npl.co.uk/events

Medical Device Technology 2007
14 - 15 February 2007
NEC, Birmingham
Come a visit the NPL stand!

International Workshop on Monte Carlo Codes
26 - 27 March 2007
NPL, Teddington

13th UK Monte Carlo User Group Meeting (MCNEG 2007)
28 - 29 March 2007
NPL, Teddington

Clinical Temperature Measurement and Thermography
2 - 3 May 2007
All Nations Centre, Cardiff
www.ipem.org.uk

Exclusive event

36th Symposium of the Ultrasonics Industry Association 19 – 21 March 2007

The UIA (Ultrasonics Industry Association) is a worldwide group of manufacturers, users and academics interested in ultrasound and its applications.

The Symposium, which is being held outside the USA for the first time in over 20 years, will cover topics such as: ultrasonic cleaning, sonochemistry and HIFU (High Intensity Focussed Ultrasound). Delegates will be given a tour of NPL's extensive laboratories.

For further details and to register for this event please visit www.ultrasonics.org/symp2007.html

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