



THE NEWSLETTER OF MALAYSIAN ORTHOPAEDIC ASSOCIATION

LETTER FROM THE EDITORIAL SECRETARY



Greetings from the Malaysian Orthopaedic Association (MOA) editorial board!

In this edition of our newsletter, Berita Ortopedik, we wish to present a special release on the activities and news from the Research Special Interest Group as part of our effort to disseminate the developments of this area within our society.

I am proud to mention here that this SIG have been actively involved in promoting orthopaedic research amongst the orthopaedic fraternity and that I also thank you all for your contributions.

We hope that other specialties will follow suit, and that with such reporting; we are able to tell everyone of our involvement in building a strong society. However, this can only happen if we receive contributions from our members who are actively involved in orthopaedics related activities. As the head of the editorial team, I am very appreciative of the contributions made by our members and hope to receive more in terms of support in order for us to highlight the society's effort to promote orthopaedics and of our contribution to society. It is our hope that we are able to tell more to the people of our commitment to the public and of our contribution towards building our nation; and therefore we hope that our member will support us by contributing good write ups.

Thank you all for your support and we look forward to hearing from all our members.

Editorial Secretary 2019/2020 Prof. Dr. Tunku Kamarul Zaman Bin Tunku Zainol Abidin

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Brief Report on Research Training Program for Clinical Student

Date January – December 2017

Venue

Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya

About the Workshop

Masters of Orthopaedics Surgery is a sought after and comprehensive postgraduate program which involves four years of clinical and research training. The students need to complete an orthopaedic research project and produce a written thesis/dissertation or alternatively publish a scientific article, before being allowed to proceed for the final examination in the final year.

The Orthopaedic Research Program was therefore established. It is a complementary research course for clinical postgraduate candidates. This program was developed to provide interested students with an opportunity to acquire skills and concepts inherent in the basic science or clinical research experience. It is intended to teach students to be creative, careful, patient and exacting in their methods of study and clinic/ laboratory investigations. It also promotes insight and analytical needed and skills addresses matters of public concern.

We improved the program in several aspects since August 2017 compared to similar events in 2016 and early of 2017, including the content of the modules and evaluation of each module and the speakers. The new amended program contains 10 modules and is divided to 2 parts: lectures and workshop/discussion for each module. This is to ensure the quality of the program is increasing. There were an average of 5 local speakers and 20 clinical orthopaedic students (in-campus and out-campus) in each class.

Successful completion of this program will signify that the student has successfully completed a course of postgraduate training in orthopaedic research under academic supervision and guidelines, and has submitted a qualified thesis that University of Malaya declares to be a contribution to knowledge and which demonstrates the student's capacity to carry out independent research, including data analysis and scientific writing.

Prepared By : Ms Rabiatul Adawiyah Othman Course Secretary

Topics in Orthopaedic Clinical Master Research Program 2017

Dates	Lecture Topic
23 February 2017	Scientific Writing
26 April 2017	Research Methodology
23 May 2017	The Literature Review: the How, Why and Wherefore
22 June 2017	Research Design
26 July 2017	Rationalizing Scientific Research
24 August 2017	Literature Review: Conducting Literature Search And Writing A Good Review
27 September 2017	Research Ethics: Introduction And Guidance To Conduct Research
25 October 2017	Research Funding And Awards: Applying For Research Funds And Knowing What Is Available
27 November 2017	The Importance Of Knowing The Regulations And Laws Relating To Doing Scientific Research



STATISTIC

Coordinator Local Speaker Dr Nam Hui Yin (NOCERAL) 5 **Participants**

20





Brief Report On Understanding Fluorescence Using Confocal Microscopy

Date 18 May 2017

Venue

 Bilik Puspasari, 1st Floor, Main Tower, University Malaya Medical Centre (Lecture) Electron Microscope Room (Hands-On)

About the Workshop

This workshop was aimed to introduce the latest technology and capability of Spectral Confocal Laser Scanning Microscope. The other objectives of the workshop are to understand the theory on basic microscopy and confocal microscopy and to share the operations, applications, tips and tricks of fluorescence imaging and microscopy.

A total of 20 participants attended this workshop. They were from Taylor's University, Sunway University, Monash University and University of Malaya. In addition, we were glad to have Dr. Anwar Norazit (University of Malaya), Dr Chong Pan Pan (University of Malaya) and Ms. AC Yuen (High-Tech Instrument Sdn. Bhd.) as invited speakers to deliver the talks. Topics that have been discussed include basics of fluorescence imaging, introduction & principles of confocal microscopy and applications of fluorescence & confocal imaging. Moreover, hands on and sample analysis trials were conducted by Ms AC Yuen.

This workshop was jointly organized between National Orthopaedic Center of Excellence for Research & Learning (NOCERAL) and High-Tech Instruments Sdn. Bhd.

Prepared By : Ms Rabiatul Adawiyah Othman Course Secretary



Photo 1: Group Photo Session



Photo 2: Lecture session; presented by Dr Chong Pan Pan and Ms AC Yuen



Photo 3: Hands on and sample analysis

STATISTIC					
Chairman	Dr C	Chong Pan Pan(TEG, NC	CERAL)	
Local Speaker	3	Committee	1	Participants	20





Event

Brief Report on Orthopaedic Specialty Committee Part 1 Preparatory Course: Pathology, Biomaterials and Biomechanics, Principles of Surgery

Date 2 - 3 July 2017

Venue Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya





Photo 1: Teaching session by Dr. Amreeta

About the Workshop

This workshop was aimed to give training and lecture to medical doctors who will take the Orthopaedic Specialty Committee. The preparatory course was coordinated by Dr. Chong Pan Pan, senior lecturer from Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya.

The event was jointly organized by NOCERAL. The invited speakers were Prof. Dr. Tunku Kamarul, Assoc. Prof. Azura Mansor, Assoc. Prof. Dr. Mun Kein Seong, Dr. Amreeta Dhanoa and Dr. Faissal Yasin from University of Malaya. There were 23 doctors who successfully completed this 2-day workshop from various hospitals.

Topics that have been discussed include the Normal Cell, Cellular Injury And Tissue Response To Injury, Genetic And Pediatric Disorders; Environmental Diseases; Diseases Of Ageing, Fluid And Hemodynamic Derangements; Renal System, Biomaterials, Vascular Disorders, Respiratory System; Cardiovascular System, Musculoskeletal System, Gastrointestinal Disorders; Liver And Biliary Tract; Pancreas, Haematopoietic System; Endocrine System; The Breast; The Male Genitalia, Immune System; Infections Perioperative Management; Emergency Medicine And Trauma; Biomechanics; Clinical Microbiology; Neoplasia; Principles Of Oncology; Surgical Techniques And Technology; And Good Clinical Practice And Legal Issues.

At the end of the course, the participants were able to identify, recognize and manage clinical problems effectively with an up-to-date knowledge.

Prepared By :

Ms Rabiatul Adawiyah Othman Course Secretary

		STATISTIC	
Chairman	Dr Chong Pan Pan (NOCERAL)		
Speakers	8	Participants	19



Brief Report on Conjoint Board of **Orthopaedic (CBO) Part 1/Basic Science Examination (BSE) Preparatory Course: Anatomy and Applied Surgical Anatomy**

17 - 18 July 2017 Date

Venue

Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya



About the Workshop

This is a monthly preparatory course for the participants who will take the Conjoint Board of Orthopaedic (CBO) Part 1/ Basic Examination Sciences (BSE). The preparatory course was coordinated by Dr. Chong Pan Pan, senior lecturer from Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya.

The event was jointly organized by NOCERAL. The invited speakers were Prof. Dr. Normadiah Kassim, Dr. Intan Suhana Binti Zulkafli, Prof. Dr. Tunku Kamarul Zaman, Dr. Snehlata Samberkar and Dr. Ganesh A/I P.vythilingam from University of Malaya, and Assoc. Prof. Dr. Lakshmi Selvaratnam from Monash University Malaysia.

There were 28 participants completed successfully this 2-day course. Topics that have been discussed include upper limb, lower limb, abdomen, pelvis, head, neck, back, thorax, basic embryology of limbs & spine, histology of musculo-skeletal tissues and surgical anatomy. The participants also took part in the small group discussion with the speakers.

At the end of the course, the participants were able to:-

- a. Explain the organization of structures, including the skeletal system, muscles, vessels and nerves of the limb
- b. Explain the organization of body wall, cavities and their respective organs and systems C. Describe the structural
- characteristics and functions of the various body tissues
- d. Explain the basic embryological development of the various organs and systems
- Correlate the anatomical e. knowledge with relevant clinical conditions.



Photo 2: Small group discussion





Prepared By :

Ms Rabiatul Adawiyah Othman Course Secretary

		STATI	STIC		
Chairman	Dr (Chong Pan Pan (I	NOCER	AL)	
Local Speaker	6	Committee	2	Participants	28



Brief Report on ELISA Workshop

Date 15 December 2017

Venue

Lecture Hall Datin Bagayah Level 2 National Orthon

e Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya

About the Workshop

This hands-on workshop was aimed to provide training to medical doctors and researchers on ELISA. This is essential to support basic laboratory knowledge for researchers and medical students. A detailed introduction about the basic ELISA protocol followed by a hands-on trial in the lab was provided by a group of Tissue Engineering scientists and technical experts of Prima Nexus Company.

The event was organized by Associate professor Dr. H.Balaji and Dr. Murali Malliga Raman of Tissue Engineering Group, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya. There were 10 participants from University of Malaya and other medical colleges of Kuala Lumpur who successfully completed 1-day workshop and the feedback given were also satisfactory.

Topics such as Western blot and other ELISA methods were also discussed. The event was jointly organized by NOCERAL and Prima Nexus Technical expert team for ELISA.



Photo 1: Lecture session

Prepared By : Ms Rabiatul Adawiyah Othman Course Secretary



Photo 2: Sample preparation



Photo 3: ELISA reader usage



Photo 4: Results analysis

STATISTIC

CoordinatorAssoc. Prof. Dr. Balaji Hanumantharao
Raghavendran (NOCERAL)Local Speaker1Participants10



Brief Report on Basic Quantitative Real-Time PCR Hands-On

Date 21 - 22 December 2017

Venue Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya Orthopaedic Molecular and Biological Laboratory (OMBL)

About the Workshop

The aims of this real-time quantitative polymerase chain reaction (qPCR) workshop are to provide the basic understanding in the qPCR principles, the complete aPCR work flow and the minimum information required for publishing the gPCR results. This workshop targeted to train basic science researchers, including research assistants (RAs), postgraduate students, post-doctoral researcher fellows, laboratory technicians and academic staffs who are interested in basic science research, especially in molecular biology. Most of the high impact basic science journals with good reputation would require authors to submit their research findings supported by, at least qPCR analysis. Hence, qPCR is a wildly used research tool, and there is increasing demand in qPCR hands-on training workshop. This workshop is essential to support increasing demand for the use of this qPCR platform in various research.

The event was iointly organized by Tissue Engineering Group (TEG), Malaysia Orthopaedic Association (MOA), Biomed Global, and NOCERAL. It was chaired by the Head of Tissue Engineering Group (TEG), Prof. Dr. Tunku Kamarul Zaman. The workshop coordinator is Dr. Tan Sik Loo. It is the first qPCR workshop conducted by TEG, NOCERAL, and it was able to attract a good number of 30 participants from various institutions, including University Malaysia Kebangsaan (UKM), Pusat Perubatan UKM (PPUKM), Universiti Putra Malaysia (UPM), Sunway University, University Sains Islam Malaysia, and Prima Nexus Sdn Bhd, apart from the from participants University of Malaya (UM). Among these 30 participants, there were 24 postgraduate students, 3 lecturers, 1 veterinary officer, 1 science officer and 1 project coordinator. Due to the limited space in the laboratory for hands-on session and to ensure the effectiveness of the hands-on session, this workshop could not take in too many participants. The workshop received an overwhelming response or request to participate in the hands-on session. In fact, there were some participants who miss the handson workshop hence requested the

workshop committee to organize another hands-on workshop in the near future.

Topics covered in this workshop include:

- a. The basic principles of polymerase chain reaction (PCR) and real-time PCR;
- b. The experimental design of a real-time PCR assay and its workflow from sample preparation to data analysis;
- c. The principle of gene expression analysis;
- d. The Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE Guidelines).
- e. Hands-on session for the complete aPCR assay workflow. from sample preparation to optimization and validation.



Photo 1: Group photo

STATISTIC Dr Tan Sik Loo (NOCERAL) Coordinator Local Speaker 1 Committee 4

10 participants attended for lecture only;

20 participants attended for both lecture and hands-on workshop.

Brief Report on Research Training Program for Clinical Student

Date 18 January 2018

Venue Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya Orthopaedic Molecular and Biological Laboratory (OMBL)

About the Workshop

The aims of this Bioanalyzer Svstem Hands-on workshop provide the basic are to understanding in capillary-based gel electrophoresis system for analyzing DNA, RNA and protein samples. This workshop was targeted to train the basic science researchers, including research assistants (RAs), postgraduate students, post-doctoral research fellows, laboratory technicians and academic staffs who are interested in basic science research, especially in molecular biology aspect. Most of the high impact basic science journals with good reputation would require authors to submit their research findings supported by, at least qPCR analysis. RNA is the sample required for qPCR analysis, where the quality and quantity of RNA sample is very crucial. Hence, Bioanalyzer system is a widely used research tool, especially for RNA analysis, thus there is an increasing demand in the Bioanalyzer System hands-on training workshops. This workshop is essential to support the increasing demand for the use of capillary-based platform in RNA quantification and quality checking.

The event was jointly organized by Tissue Engineering Group (TEG), Malaysia Orthopaedic Association (MOA), NeoScience Sdn Bhd, and NOCERAL. It was chaired by the Head of Tissue Engineering Group (TEG), Prof. Dr. Tunku Kamarul Zaman. The workshop coordinator was Dr. Tan Sik Loo. It was the first Bioanalyzer System Handson workshop conducted by TEG, NOCERAL, and it was able to attract a good number of 12 participants

from the University of Malaya (UM). Among these 12 participants, there were 4 participants who registered for the hands-on session. All participants were either the postgraduate research students research assistants or and Medical Laboratory Technologists. Although very small number participants were involved of the hands-on session, the in effectiveness of the hands-on session was assured.

Topics covered in this workshop include:

- a. The basic principles of capillary based electrophoresis for DNA, RNA and protein samples;
- b. The hands-on technique for analysing RNA quality using 2100 Bioanalyzer system and RNA 6000;
- c. The data analysis for the RNA 6000 RNA results. 🔟



Photo 1: Group photo session



Photo 2: Data analysis discussion session

STATISTIC

Coordinator Dr Tan Sik Loo (NOCERAL)

Local Speaker 1 Committee

12 participants attended for lecture only;

4 participants attended for both lecture and hands-on workshop.

2





Brief Report on Orthopaedic Specialty Committee (OSC) Part 1 Preparatory Course: Anatomy and Applied Surgical Anatomy

Date 4 - 5 June 2018

Venue Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya

About the Course

This is a monthly preparatory course for the participants who will take the Orthopaedic Specialty Committee (OSC) Part 1. The preparatory course was coordinated by Dr. Chong Pan Pan, senior lecturer from Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya.

The event was jointly organized by NOCERAL. The invited speakers were Prof. Dr. Normadiah Kassim, Dr. Intan Suhana Binti Zulkafli, Prof. Dr. Tunku Kamarul Zaman from University of Malaya,Assoc. Prof. Dr. Ahmad Fadzli Sulong from International Islamic University Malaysia and Assoc. Prof. Dr. Lakshmi Selvaratnam from Monash University Malaysia.

There were 16 participants who were successfully completed this 2-day course. Topics that have been discussed were including upper limb, lower limb, abdomen,



Photo 1 & 2: Small group discussion by Prof. Dr. Normadiah

pelvis, head, neck, back, thorax, basic embryology of limbs & spine, histology of musculo-skeletal tissues and surgical anatomy. The participants also took part in small group discussion with the speakers.

At the end of the course, the participants were able to:-

- a. Explain the organization of structures, including the skeletal system, muscles, vessels and nerves of the limb
- b. Explain the organization of body wall, cavities and their

respective organs and systems

- c. Describe the structural characteristics and functions of the various body tissues
- d. Explain the basic embryological development of the various organs and systems.
- e. Correlate the anatomical knowledge with relevant clinical conditions.

Prepared By : Ms Rabiatul Adawiyah Othman Course Secretary



Photo 3 & 4: Small group discussion by Dr Intan Suhana

STATISTIC

ChairmanDr Chong Pan Pan (NOCERAL)Local Speakers5Committee2Participants16



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Event

Brief Report On The CBO Part 1/Basic **Sciences Examination Preparatory Course: Physiology And Applied Clinical Physiology**

9 - 10 July 2018 Date

Venue

Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya



About the Workshop

This is a montly preparatory course for participants who will take the Orthopaedic Specialty Committee (OSC) Part 1. The preparatory course was coordinated by Dr. Chong Pan Pan, senior lecturer from Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya.

The event was jointly organized by NOCERAL. The invited speakers were Prof. Dr. Tunku Kamarul Zaman, Prof. Dr. Ruby Husain and Dr Raja Elina Afzan Raja Ahmad from University of Malaya and Prof. Dr. Norfilza Mohd Moktar from Universiti Kebangsaan Malaysia.

There were 32 participants who were that successfully completed this 2 days course. Topics that have been discussed were including muscle and neuromuscular junctions, respiratory system, acid base balance, body fluid and electrolytes physiology, nervous system, blood and hematologic system, cardiovascular system, renal system, endocrine system, alimentary system, cellular physiology and miscellaneous topics. The participants also took part in small group discussion with the speakers.

At the end of the course, the participants were able to:

- a. Explain the cellular and molecular basis of the excitability of the nervous system
- b. Identify the source of compensation for blood pH

problems of a respiratory origin

- Distinguish between the types C. of cells that compose nervous tissue
- d. Understand the neural and hormonal regulation of diaestion
- Describe the components of e. blood and volume control in relation to the hematopoietic system. 🔟

Prepared By :

Ms Rabiatul Adawiyah Othman **Course Secretary**



		STATISTIC	
Chairman	Dr C	Chong Pan Pan (N	IOCERAL)
Speakers	4	Participants	32





Brief Report On Unleash Your Research Potential With Advances In Flow Cytometry

Date 7 - 8 August 2018

Venue

ue Lecture Hall Datin Ragayah, Level 2, National Orthopaedic Center of Excellence for Research & Learning, Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya

About the Workshop

The event was jointly organized by Tissue Engineering Group, (NOCERAL), Straits Scientific and Beckman Coulter Life Science. It was coordinated by Dr Chong Pan Pan. It is the first workshop conducted by Straits Scientific and it was able to attract 7 participants from University of Malaya, 2 participants from International Islamic University Malaysia, 1 from Universiti Sains Malaysia and 1 from University of Edinburgh. Amongs of these participants, 5 of them who registered for handon session. All the participants were either associate professors, PhD students or master students. Although a very small number of participants were involved in the hands-on session, the effectiveness of the hands-on session was assured.

Topics covered in the workshop were including:

- a. Introduction to the Principle of Flow Cytometry
- b. Flow Cytometry Applications MSC Immunophenotyping, Cell Cycle & Necrobiology
- c. CytoFLEX: The Next Gen Flow Cytometry
- d. Flow Cytometry Briefing Cell Cycle & Apopotosis 🔤



Photo 1: Group Photo session









Prepared By : Ms Rabiatul Adawiyah Othman Course Secretary

STATISTIC

Chairman	Dr Chong Pan Pan (NOCERAL)		
Speakers	2	Participants	11





Platelet Rich Plasma (PRP) As An Orthobiologics: A Short Ariticle On What You Need To Know As An Orthopaedic Practitioner Article by Tunku Kamarul Zaman

For many years now, platelet rich plasma (PRP) has been widely used by physicians as a method for treating various medical conditions. PRP, as what it is most commonly known, is a biological product defined as a portion of the plasma fraction of autologous blood with a platelet concentration above the baseline (before centrifugation). As such, PRP contains not only high levels of platelets but also the full complement of clotting factors; the latter typically remaining at their normal, physiologic levels. PRP is enriched by a range of growth factors, chemokines, cytokines, and other plasma proteins that makes it useful for regenerating cells and tissues. In many conditions, the use of PRP has resulted in good outcomes such as the in treatment of non-united fractures and tendinitis. PRP is easy and safe to produce, and because it can be administered easily even in the clinic settings, PRP has been generously prescribed by surgeons and physicians alike.

Sadly though, there are parties who are presently using PRP indiscriminately; many of which are applied in conditions that may not be medically indicated. This includes injections for pure cosmetics reasons. As PRP become increasingly accessible to doctors (and others in related industries), its use has become rampant to a point where PRP itself has become a common household name. For the public, PRP is perceived as a cheap alternative to surgery, almost like a miracle injection; And because there is so much interest and demand from the public, the industry relating to PRP has flourished with more and more companies introducing new techniques and new products that promise superior outcomes. The question is, how effective is this treatment and what does it mean to an orthopaedic surgeon? Are the claims of its regenerative potential true? Can it be used for our patients?

Whilst the topic relating to PRP can be discussed and debated endlessly, it is my hope that a short article such as this can help to enlighten some of the key points necessary for a practicing orthopaedic surgeon to understand what PRP is in order for them to make sensible recommendations to his or her patients.

How Did The PRP Industry Started?

Whilst the exact origin of PRP remains to be determined, it has been long suggested that the concept

and description of PRP started in the field of hematology. We also know that hematologists created the term PRP in the 1970s in order to describe the plasma with platelet count above that of peripheral blood. Back then, physicians created PRP with the intention to be used as a transfusion product to treat patients with thrombocytopenia. Although this product never became a hit for hematologists, ten years later, PRP started to be used in maxillofacial surgery. Known initially as PRF ("F" referring to Fibrin since



Image illustrating how PRP is used in treating cartilage disease of the knee; Adapted from Knop et al., Rev Bras Reumatol. 2016; 56(2): 152-164



Image adapted from published works by Samuel S et. Al. demonstrating that when platelets are activated, these cells degranulation their content that are enriched with growth factor particles. It is these factors that is said to produce the beneficial effects, namely tissue regeneration.

it is thought to have the potential for adherence and homeostatic properties), this term gradually became interchangeable with PRP. Subsequently, PRP has been used in, predominantly, musculoskeletal conditions especially in sport injuries. With its use in professional sportspersons, it has attracted widespread attention in the media and has been extensively used in this field. Other medical fields now also have joined in to utilize this product which includes cardiac surgery, paediatric surgery, gynaecology, plastic surgery and many others.

The effects of economics of scale and the reduction of cost over time have resulted in PRP being made more accessible to not only to the doctors, but also to the patients themselves as injections of PRP become cheaper and more affordable. Several decades ago when PRP was first introduced to healthcare professionals, the machines used to process PRP was excessively priced, allowing only very few well funded institutions to be able to provide PRP as a service. Today, machines used to produce PRP are relatively cheap, allowing small time general practice clinics, office-lot wellness centers and even private owners to be able to produce PRP, albeit of varying standards.

How Does PRP Work?

Platelets contain several secretory granules that are crucial for platelet function. There are 3 types of granules: dense granules, o-granules, and lysosomes. In each platelet there are approximately 50–80 granules, the most abundant of the 3 types of granules. These granules makes PRP an attractive natural source of signaling molecules, and

upon activation of platelets in PRP, the P-granules are degranulated and release the GFs and cytokines that will modify the pericellular microenvironment. Some of the most important GFs released by platelets in PRP include vascular endothelial GF, fibroblast GF (FGF), platelet-derived GF, epidermal GF, hepatocyte GF, insulin-like GF 1, 2 (IGF-1, IGF-2), matrix metalloproteinases 2, 9, and interleukin 8. In several studies there were at least 90 different proteins identified in PRP which may influence cellular and tissue regeneration.

How Do You Obtain PRP?

There are many techniques describing how PRP can be obtained from the peripheral blood. Some of which are complicated whilst others are very simplistic. In general, these techniques adopt the same principal, i.e. to centrifuge the blood to a point where the plasma is separated from the red blood cells, and that platelets are extracted from the plasma region taking with it the most minimal amount of plasma as possible: The smaller the plasma volume taken, the higher the concentration of PRP

PRP is obtained from a sample of patients' blood drawn at the time of treatment. A 30 cc venous blood draw will yield 3-5 cc of PRP depending on the baseline platelet count of an individual, the device used, and the technique employed.



Images above help to illustrate a commonly used method to extract PRP from peripheral blood. Images are with courtesy from PP Chong et. Al.

Outlook

The blood draw occurs with the addition of an anticoagulant, such as citrate dextrose A to prevent platelet activation prior to its use. Following centrifugation, 3 basic layers can be observed: at the bottom of the tube, there are red blood cells with leukocytes (or white blood cells) deposited immediately above; the middle layer corresponds to the PRP, and at the top, there is the Platelet poor plasma (PPP). The PPP is removed, and PRP is obtained.

Platelets can be activated before the application of the PRP and is said to provide superior outcomes when done so. Thrombin and calcium chloride are known aggregation inducers and have been used to activate platelets and stimulate degranulation, causing the release of the GFs into the targeted site. Whether or not the use of agitators is truly superior remains debatable, although logic dictates that such actions may be justified.

Does Different Types Of PRP Exists?

In principal, PRP can be categorized further to "different" preparations when several processes are added to the original method of producing PRP. According to the classification proposed by Ehrenfest et al. (2009), four main families of preparations can be defined, depending on their cell content and fibrin architecture.

- i. Pure Platelet-Rich Plasma (P-PRP) or leucocyte-poor PRP products are preparations without leucocytes and with a low-density fibrin network after activation.
- ii. Leucocyte- and PRP (L-PRP) products are preparations with leucocytes and with a lowdensity fibrin network after activation. It is in this family that the largest number of commercial or experimental systems exists. Particularly, many automated protocols have been developed in the recent years, requiring the use of specific kits that allow minimum handling of the blood samples and maximum standardization of the preparations.

- iii. Pure platelet-rich fibrin (P-PRF) or leucocyte-poor plateletrich fibrin preparations are without leucocytes and with a high-density fibrin network. These products only exist in a strongly activated gel form, and cannot be injected or used like traditional fibrin glues.
- iv. Leucocyte- and platelet-rich fibrin (L-PRF) or secondgeneration PRP products are preparations with leucocytes and with a high-density fibrin network.

In addition to the above, newer variants of PRPs have been mentioned such as Platelet Extra Cellular Vesicles (PEV) and Autologous Conditioned Plasma (ACS). Based on my own experience, over the years there have also been claims of a superior version of PRPs against another. This remains to be debated.

Is One PRP Preparation Better Than The Other?

In order to make a clear conclusion that one treatment is superior to another, a very well designed and stringent double (or triple, or even blinded randomized quadruple) controlled trial (RCT) needs to be performed, involving many patients of varying demographics. At present, there are no such studies reported. At best, we are able to observe several reports from meta-analyses and systematic reviews on a wide variety of indications adopting varying techniques and preparations, not to mention the variation in the stages of disease presentation, the patient demographics, and many other factors. Hence, although it appears to suggest that some techniques may be better, no conclusion can be made. Even then, when we consider the reports of the use of PRP, we have yet to see large series of studies comparing PRP treatment to non-PRP treatment in robust RCTs. This makes it difficult for a convincing argument to be made for the endorsement of the use of PRP as a mainstream treatment for an indicated medical condition.

Whilst there are many who claim that there is a superiority of one preparation over another, and that if we were to discuss this would take too large a document to be published in this short newsletter, there is no concrete evidence to prove as such. It is quite understandable that any inventor would want to promote his or her own product over another; therefore such claims are not unexpected.

The Verdict:

PRP is an acceptable tool to be used in clinical practice due to its long-standing track record of safety and selective efficacy. Together with lower cost, PRP will continue to be used beyond its intended indications despite the lack of concrete evidences to support its use especially in untested conditions. It is difficult to promote one preparation over the other due to the lack of presently supporting substantive data, and more so for the treatment it is used. As such, there appears to not be a simple "yes" or "no" answer to the various issues in PRP. Inevitably, it boils down to the doctors who are responsible in treating their patients. With the evidences presented at hand, it would therefore be paramount for a doctor to convey the most accurate information to the patient in order for them to give informed consent, and to advice them on what could be best for them. After all it is the doctor's job to safeguard the patient's interest when it involves their health and well-being. 🔤

The author of this article:

Disclaimer: The article represents the opinion of the writer and does not reflect the opinion or policies of MOA.

Prof. Dr. Tunku Kamarul Zaman is the Head of the Tissue Engineering Group from the National Orthopaedic Center of Research and Learning (NOCERAL) located in University of Malaya. He is also the Chairman of the Asia Pacific Orthopaedic Research Society and is the co-author of several articles relating to PRP and research related to this subject.



Question 1

This is a membrane potential curve of a neuronal cell following a stimulus (at the green arrow) with the different regions of the graph indicated by alphabets.

- I. Name regions A, B, C, D, E and what this region signifies.
- II. A certain level of stimuli is needed before region B can occur. What is that level known and approximately what is the value?
- III. Explain the ionic changes occurring in and outside the cell when an appropriate stimulus is provided sufficiently to create the phenomenon observed in region B?

Answer:

- I. Regions of the image:
 - A. The resting state: For quiescent cells, the relatively static membrane potential is known as the resting membrane potential. The resting membrane potential is at equilibrium since it relies on the constant expenditure of energy for its maintenance. It is dominated by the ionic species in the system that has the greatest conductance across the membrane. For most cells, this is potassium. As potassium is also the ion with the most-negative equilibrium potential, usually the resting potential can be no more negative than the potassium equilibrium potential.
 - B. Depolarization: A stimulus from a sensory cell or another neuron depolarizes the target neuron to its threshold potential (-55 mV), and Na+ channels in the axon hillock open, starting an action potential. Once the sodium channels open, the neuron completely depolarizes to a membrane potential of about +40 mV. The action potential travels down the neuron as Na+ channels open. Positive ions flood the interior of the neuron and depolarize the membrane, decreasing the difference in voltage between the inside and

outside of the neuron. A stimulus from a sensory cell or another neuron depolarizes the target neuron to its threshold potential (-55 mV), and Na+ channels in the axon hillock open, starting an action potential. Once the sodium channels open, the neuron completely depolarizes to a membrane potential of about +40 mV.

- C. Action potential: Transmission of a signal within a neuron (in one direction only, from dendrite to axon terminal) is carried out by the opening and closing of voltage-gated ion channels, which cause a brief reversal of the resting membrane potential to create an action potential. As an action potential travels down the axon, the polarity changes across the membrane. Once the signal reaches the axon terminal, it stimulates other neurons.
- D. Repolarization: At the peak of the action potential, the sodium permeability is maximized and the membrane voltage is nearly equal to the sodium equilibrium voltage. However, the same raised voltage that opened the sodium channels initially also slowly shuts them off, by closing their pores; the sodium channels become inactivated. This lowers the membrane's permeability to sodium relative to potassium, driving the membrane voltage back towards the resting value. The changes in sodium and potassium permeability cause the repolarization of membrane and producing the "falling phase" of the action potential.
- E. Hyperpolarization: The diffusion of K+ out of the cell hyperpolarizes the cell, making the membrane potential more negative than the cell's normal resting potential. At this point, the sodium channels return to their resting state, ready to open again if the membrane potential again exceeds the threshold potential. Eventually, the extra K+ ions diffuse out of the cell through the potassium leakage channels, bringing the cell from its hyperpolarized state back to its resting membrane potential.
- II. Threshold level of excitation. This level is approximately at -55mV.
- Action potentials are caused when different ions iii. cross the neuron membrane. A stimulus first causes sodium channels to open. Because there are many more sodium ions on the outside, and the inside of the neuron is negative relative to the outside, sodium ions rush into the neuron. Sodium has a positive charge, so the neuron becomes more positive and becomes depolarized. It takes longer for potassium channels to open. When they do open, potassium rushes out of the cell, reversing the depolarization. Also at about this time, sodium channels start to close. This causes the action potential to go back toward -70 mV (a repolarization). The action potential actually goes past -70 mV (hyperpolarization) because the potassium channels stay open a bit too long. Gradually, the ion concentrations go back to resting levels and the cell returns to -70 mV.

Trainee Quick Quiz

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Question 2

A 20-year-old worker fell from a high ladder while painting a wall, resulting in severe pain over his right wrist. There were no other noticeable injuries except for some bruising and cuts to his elbows and back. His right hand was put on a splint and he was later sent for radiography investigation.

- I. Describe the findings of the radiograph above.
- II. Name the injury (diagnosis) and explain the mechanism that resulted in this injury.
- III. What is the aim of the treatment for this condition?
- IV. Name the most common classification used for this injury?

Answers:

- I. Fracture of the scaphoid, lunate dislocation volarly and dorsal displacement of the distal carpus row.
- II. Trans-scaphoid perilunate dislocation. Occurs due to high-energy trauma with the hand in the outstretch position.
- III. The treatment aims at reducing dislocation, internally fixing the fracture, and repairing ligament injuries. It is hoped that doing so will reduce the likelihood of developing traumatic arthritis of he carpal joint.

- IV. Although there are no specific classifications used for this condition, most often the Mayfield classification has been applied. Mayfield classification of carpal instability, also known as perilunate instability classification (carpal dislocations), describes carpal ligament injuries. Instability has been divided into four stages:
 - A. Stage I: scapholunate dissociation (rotatory subluxation of the scaphoid): Disruption of the scapholunate ligament with resultant Terry Thomas sign. Exacerbated in clenched fist views
 - B. Stage II: perilunate dislocation: The lunate remains normally aligned with the distal radius, and the remaining carpal bones are dislocated (almost always dorsally). The capitolunate joint is disrupted, and the lunate projects through the space of Poirier. 60% are associated with scaphoid fractures
 - C. Stage III: midcarpal dislocation: lunotriquetral interosseous ligament disruption or triquetral fracture. Neither the capitate nor the lunate is aligned with the distal radius.
 - D. Stage IV: lunate dislocation. Dorsal radiolunate ligament injury. Dislocation of the lunate in a palmar direction. Tipped teacup appearance.

Disclaimer: The case described is fictitious and the images we randomly taken from the Internet for illustration purposes only. Any resemblances to any individual or cases that has occurred to person presently living or dead incompletely unintentional.