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聖保祿醫院
St. Paul's Hospital

NewsLetter
院訊

Transarterial Radioembolization with Y90 Microsphere

Hospital Updates:

- Anticoagulants
- New Drugs Available at SPH

MESSAGE
FROM THE MEDICAL SUPERINTENDENT

Dr. William Ho
Medical Superintendent

Credentialing for Patient Safety

Ever since hospitals in Hong Kong embarked on accreditation from the Australian Council of Healthcare Standards (ACHS) scheme, Credentialing has been a buzzword. One reason is that this is a recent development locally. But even Australian hospitals may not be ahead of us so much either, for the simple reason that this is both a difficult as well as a contentious area.

In simple terms, Credentialing is the process of vetting evidence to form a view about a clinician's sphere of competence in providing clinical services. There is a parallel process of Privileging, or Defining Scope of Service – i.e. determining who can do what. E.g. who are allowed to do colonoscopies, or percutaneous coronary interventions (PCI), or hysterectomy in the hospital?

Traditionally, the notion has been one of professional autonomy with the doctors answering to themselves and the Medical Council only. The implicit safeguard in public hospitals is that doctors are under a structure of clinical supervision. In the private sector, hospitals are merely seen as passive platforms for private doctors to treat patients. These notions are no longer tenable in this day and age of corporate governance and clinical accountability. One cannot assume that doctors always stick to areas where they are adequately trained and keeping updated knowledge and skills on, especially given the money incentive.

One option is for hospital management to dictate – private hospitals always have absolute discretion to approve or disapprove doctor privileges. By itself this is not adequate. The professional scene is changing fast, both in terms of training and practice. In St. Paul's Hospital (SPH), we are partnering with clinicians in various Clinical Advisory Committees to provide peer consensus in recommendations to hospital management.

The principles are always based on training and proof of experience. E.g. general surgeons in the old days may indeed have done a lot of urology work as well, while those trained after the two streams split off would not be competent in the latter. On the other hand, certain new procedures like endobronchial ultrasound (EBUS) only appeared in recent years. Doctors of the relevant specialty would not be automatically granted such procedure privileges unless there is proof of training or experience. In addition to professional competence, the hospital may also take into account character checks, like whether the applicant had been guilty of misconduct.

Hospitals would always like to have authoritative backing in these "local rules". One good example is the detailed practitioner accreditation of coloscopy levels by the Hong Kong College of Obstetricians and Gynaecologists. If the College certifies a certain doctor as having level 2 competence, that is the limit allowed for his colposcopy operations in the hospital. Unfortunately, most Colleges under most circumstances do not define as clearly. It remains for the hospital management to safeguard patient interests through proper processes of credentialing and defining scope of practice for clinicians. In SPH we are most grateful to dedicated clinical colleagues who devote their precious time in this important work, which contribute to the upholding of our collective Professionalism.

MEDICAL ARTICLE

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Specialist in Radiology
St. Paul's Hospital

Transarterial Radioembolization with Y90 Microsphere

Hepatocellular carcinoma (HCC) is one of the top leading causes of cancer. In South East Asia, it is related to the high prevalence of chronic hepatitis B related cirrhosis. The clinical course can be silent and many patients cannot receive curative resection or ablation, which may be due to big tumor size, vascular invasion or poor liver reserve.

For patients with inoperable HCC, the conventional treatment is transarterial chemoembolization (TACE). This has been proven to be beneficial and can prolong survival in suitable patients. However, TACE is not effective for big tumors and for tumors with major portal vein invasion.

Radioembolization with Y90 has been proposed as an alternative option. It is generally safe and most patients require administration of a single dose only. Clinical studies have shown the beneficial effect of RE for patients with inoperable HCC and for patients with liver dominant colorectal metastases.
Unlike most organs, liver has dual blood supply: hepatic artery and portal vein. HCC derives 80-90% of the blood supply from the hepatic artery. The fundamental concept of radioembolization is administration of brachytherapy by microspheres embedded with beta-emitting isotopes (Y90).

Patients considered for radioembolization therapy would include those with (1) unresectable hepatic primary or metastatic cancer, (2) liver-dominant tumor burden, and (3) a life expectancy of at least 3 months. In metastatic colorectal cancer, radioembolization therapy can be given (1) alone after failure of first-line chemotherapy, (2) with FUDR during first-line therapy, or (3) during first- or second-line chemotherapy on a clinical trial.

Once a patient has been selected as a candidate for radioembolization, an initial angiographic evaluation that includes abdominal aortogram, superior mesenteric and celiac arteriogram, and selective right and left hepatic arteriogram is to be performed to document the visceral anatomy, provide information on perfusional flow characteristics of the targeted vascular territory, identify anatomic variants, and isolate the hepatic circulation by occluding extrahepatic vessels. Given the possibility of nontarget deposition of microspheres, experts recommend the prophylactic embolization of all extrahepatic vessels at the time of MAA assessment, including the gastroduodenal, right gastric, and other extrahepatic vessels, to avoid extrahepatic deposition of microspheres. Pretreatment hepatic artery 99mTc MAA scan is performed to evaluate hepatopulmonary shunting.

Y90 was contraindicated if the lung shunting was more than 20%, the tumor/liver ratio was less than 4, or there was an unpreventable risk of Y90 microspheres reflux to extrahepatic arteries

Substantial data are available on the acute and late side effects of Y90 microspheres in hepatocellular carcinoma patients. It is quite common for patients undergoing Y90 microsphere therapy to experience mild postembolization syndrome on the day of treatment and for up to 3 days after treatment. Symptoms include fatigue, nausea, and abdominal pain. Radioembolization to nontarget organs can also cause other acute damage, resulting in gastrointestinal ulceration, pancreatitis, and radiation pneumonitis. Late toxicity can include radiation-induced liver disease (radiation hepatitis). The incidence of nontarget radiation will be minimized if meticulous angiographic and dosimetry techniques are used.

The two largest scale phase II studies have shown the safety of RE in HCC. In the American study of 291 patients receiving 526 treatments, the response rate was 42% by World Health Organization (WHO) criteria and 57% by European Association for the Study of the Liver (EASL) criteria. The median survival was 26.9 months, 17.2 months and 7.3 months for patients with BCLC stage A, B and C tumors. The median survival was 17.2 months for Child-Pugh A patients and 7.7 months for Child-Pugh B patients. Patients with Child Pugh B cirrhosis and portal vein thrombosis had poor outcome. In the European study involving 325 patients, the median survival was 24.4, 16.9 and 10.0 months for patients with BCLC stages A, B and C diseases. The independent prognostic factors for survival were

ECOG status, tumor burden (nodules more than 5), international normalized ratio (INR) more than 1.2, and extrahepatic disease. Other studies show similar results, the median overall survival was 16.4 months in a group of 108 patients. No lung or visceral toxicity was observed. In another group of 52 patients, the median overall survival was 15 months. Child-Pugh class and the tumor response were the variables affecting survival. There was a non-significant trend in favor of patients with no portal vein thrombus versus patients with portal vein thrombus. (18 vs 13 months).

A multidisciplinary team approach, combining the expertise and skill of various specialties, is essential in the management of patients planning for TARE. Combinations of personnel from the disciplines of interventional radiology, radiation oncology, nuclear medicine, medical physics, hepatology, surgical oncology, medical oncology, and radiation safety is needed.

In conclusion, Yttrium-90 microsphere therapy is a complex procedure that requires multidisciplinary management for safety and success. There is sufficient evidence to support the safety and effectiveness of Y90 microsphere therapy in selected patients with primary and metastatic liver cancer.

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ACCREDITATION
Updates

After a whole year of preparation and quality enhancement projects, St. Paul's Hospital was successfully awarded full accreditation for a 4-year period by The Australian Council on Healthcare Standards (ACHS) in May 2014 which certified the quality of our clinical and support services and corporate governance are in line with international standards.

The first time being accredited by the ACHS marked the milestone of St. Paul's Hospital's commitment towards quality and patient safety. The ACHS Certificate Presentation Ceremony was held on 26th August 2014 in St. Paul's Hospital. We were honored to have Mr. Stephen Walker, a member of the Board of Director of ACHS, who travelled from overseas to present the certificate. The Hospital Management team was delighted to celebrate this glorious and memorable moment with all staff who contributed tremendously in preparation of the accreditation survey.

Moon cakes were served in the ceremony to our overseas guests as the Mid-Autumn Festival was approaching.

Central line audit

Central line insertion is a common bedside procedure. International guidelines recommend that ultrasound (USG) guidance should be the standard practice for central line insertion to minimize complications. Right internal jugular vein (RIJV) is the optimal site for insertion and the usual overall success rate for puncture is quoted to be around 90% with USG guidance. We have performed an audit on central line insertion from Dec 2012 – Jan 2014. A total of 110 cases of line insertion from general ward and intensive care unit were collected. Ten doctors were involved in line insertion and majority of cases (90%) were reported to use real time USG guidance. Patients were mostly elderly with slightly more male patients (mean age: 74.1 years, males: 55.5%). The commonest indication for line insertion was poor peripheral venous access (53.6%), followed by drug therapy (25.5%)and renal replacement therapy (23.6%) (some cases had more than one indication). RIJV was the commonest site of insertion (80%) whether the doctor used USG guidance or not. The single puncture success rate for real time USG guidance was 93%. In other words, the need for multiple punctures (equal or more than two) was only 7%. Complication rate was 4% but all were unrelated to arterial puncture or pneumothorax.

Our results are in line with international benchmarks. This is important in the private hospital setting as patient satisfaction is improved due to a low incidence of multiple punctures and complications. This may also reduce the incidence of line sepsis if the line needs to be kept for a longer period of time. A portable USG machine is available in the Outpatient Department and is ready for use by doctors who would like to perform central line insertion.

HOSPITAL UPDATES

Warfarin, for many years, was the only oral anticoagulant for thromboembolic disorder or systemic embolism. Its major limitations are its narrow therapeutic window of providing adequate anticoagulation without bleeding, inter-patient dose response variability, monitoring requirements, and numerous drug-drug/food interactions. Today, more options are available for our prescribers and patients. However, are these newer oral agents necessarily more efficacious and safer than our gold standard warfarin? Let's review them one by one.

Pradaxa (Dabigatran)

Pradaxa is a prodrug that is converted in vivo to a potent direct thrombin inhibitor and inhibits coagulation by halting thrombin-mediated effects. Figure 1 highlights the key players in the coagulation cascade. In a number of studies, Pradaxa has demonstrated superior efficacy to warfarin in lowering the risks of ischemic stroke, intracranial hemorrhage, and systemic embolism. The risks for myocardial infarctions (MI) and of major gastrointestinal bleeding are slightly higher for patients on Pradaxa than warfarin.

Pradaxa is not approved for patients with atrial fibrillation (AF) caused by heart valve problems or if the patient has an artificial heart valve. In a recently published trial performed on patients with heart valve replacement, the RE-ALIGN trial, patients on Pradaxa showed higher incidences of strokes, MI, and blood clot formations on the mechanical heart valves than warfarin users. Moreover, major bleeding rates were higher in the Pradaxa group than the warfarin group in this patient population. The trial was terminated prematurely due to the above two significant findings.

A common adverse effect of Pradaxa is dyspepsia and this may limit its use in some patients. For absorption enhancement, Pradaxa capsules contain dabigatran-coated tartaric acid core. This acidity may partly explain the higher incidences of dyspepsia with the use of Pradaxa. If patients require the use of antacids while on Pradaxa, they should be advised to take Pradaxa at least two hours prior to the antacid. Another disadvantage is that Pradaxa requires twice daily dosing. An added caution with using Pradaxa is its potential for product breakdown and loss of potency from moisture; patients are to be reminded to only break the package foil immediately prior to use.

Xarelto (Rivaroxaban)

Xarelto is a factor Xa inhibitor and exerts its effect via the direct, selective, and reversible inhibition of factor Xa in the coagulation pathways. It requires only once daily dosing but doses of 15mg or higher should be taken with food; for use in nonvalvular AF, it is preferred to be taken with each evening meal. In the various trials conducted to date, Xarelto is found to be non-inferior to warfarin in non-valvular AF patients for stroke and systemic embolism prevention. Although critical, fatal, and intracranial bleeding occurred less frequently with Xarelto, it causes more hemoglobin decreases, need for transfusions, and GI bleeds than warfarin.

Eliquis (Apixaban)

Like Xarelto, Eliquis is also a factor Xa inhibitor but requires twice daily dosing with or without food. Use of Eliquis in the ARISTOTLE trial showed lower risks of hemorrhagic stroke, major bleeding, and death versus warfarin. The risk of ischemic stroke and systemic embolism was similar between the two drugs. This is the newest of the anticoagulants on the market, and therefore more studies are in the pipeline to evaluate Eliquis' safety and efficacy.

Since the launch of these three new-age oral anticoagulants, the management of anticoagulation has changed significantly. No longer is rat poison our only tool in combating thrombosis. These newer agents have a quicker onset of action and most cases do not require overlap with parenteral anticoagulant. Compared to warfarin, these newer medications require minimal monitoring in patients with stable pharmacodynamics. Moreover, these three oral anticoagulants allow patients more flexibility in food and supplementation options. Despite great advantages of these newer oral anticoagulants, careful patient selection must be considered. The newer agents are not indicated in treatment of valvular AF cases, their effects are non-reversible, have less established bleeding management protocols, most require renal adjustments, and their upfront cost can be greater to patients. A quick summary of the four discussed medications are compared in Table 1. Hopefully with more clinical trials and head-to-head comparison studies in the near future, practitioners can maximize the appropriate use of these newer agents.

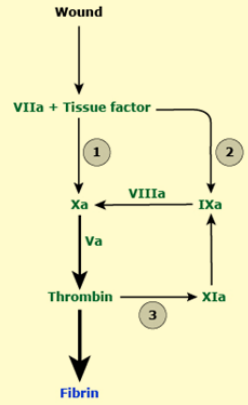

Figure 1 Coagulation Cascade (Adapted from UpToDate.com)

Table 1

Brand Name	Pradaxa	Xarelto	Eliquis	Coumadin
Generic name	Dabigatran	Rivaroxaban	Apixaban	Warfarin
Dosing:				
DVT prophylaxis after knee/hip replacement	110mg stat after surgery then 220mg daily	Off label: 10mg daily with or without food (for knee: 12-14 days/ for hip: 35 days)	2.5mg BD (for knee: 10-14 days/ for hip: 32-38 days)	Dosing based on patient's INR goal (eg. 2.0-3.0, 2.5-3.5) and lab results. Usually initiate at 2mg to 5mg daily.
DVT and pulmonary embolism treatment	150mg BD	(Also for prevention of recurrent DVT and PE) Day 1 - 21: 15mg with food Day 22 and onwards: 20mg daily with food.	Off label: 10mg BD for 7 days then 5mg BD	See above
Nonvalvular atrial fibrillation	150mg BD	20mg daily with evening meal	5mg BD	See above
Renal adjustment:				
CrCl 30 - 50 ml/min	150mg dailly	15mg daily	No dose adjustment	No dose adjustment
CrCl < 30 ml/min	Not recommended	Use with caution	2.5mg BD (use with caution)	No dose adjustment
CrCl < 15ml/min	Not recommended	Not recommended	Not recommended	Not recommended
Hepatic adjustment	Not recommended if liver enzymes > 2 ULN.	Avoid use in moderate to severe hepatic impairment with Child Pugh B and C class or patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk.	Avoid in hepatic disease with coagulopathy and bleeding risk or severe hepatic impairment. Caution if Child Pugh A or B, liver enzymes > 2 ULN, or total bilirubin > 1.5 X ULN.	Reponse to warfarin may be significantly enhanced in patients with obstructive jaundice, hepatitis, and cirrhosis. INR should be closely monitored.

Switch from warfarin	Discontinue warfarin and initiate dabigatran when INR < 2.0.	For nonvalvular AF: discontinue warfarin and initiate rivaroxaban when INR < 3.0. For DVT, PE, and prevention of recurrence: discontinue warfarin and initiate rivaroxaban when INR < 2.5.	Discontinue warfarin and initiate apixaban when INR < 2.0.	N/A
Major drug interactions	Strong P-gp inhibitors (eg. amiodarone, verapamil, quinidine, clarithromycin). Strong P-gp inducers (eg. rifampicin, St. John's wort, carbamazepine, phenytoin). Antacids.	Inhibitors of both CYP3A4 & P-gp (eg. azole-antimycotics, HIV protease inhibitors). Dronedarone. Strong CYP3A4 inducers (eg. rifampicin, carbamazepine).	Strong inhibitors of both CYP3A4 & P-gp (eg. azole-antimycotics, HIV protease inhibitors). Strong inducers of both CYP3A4 & P-gp (eg. rifampicin, carbamazepine, phenobarbital).	Numerous food and drug interactions; refer to product's labeling information
Hold prior to elective surgery or invasive procedures with risk of bleeding	At least 24hrs to 48 hrs before.	At least 24 hrs before.	At least 24hrs to 48 hrs before.	At least 5 days before.

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8. Product monographs.

After Drug and Therapeutics Committee (DTC) Meeting in September 2014, the following new drugs are approved:

Approved drugs	Indication(s)	Usual dosage	Note
Orencia (Abatacept) injection 250mg IV infusion 125mg pre-filled syringe	Biological agent for treating rheumatoid arthritis (RA) and juvenile idiopathic arthritis (JIA)	IV infusion- dose is according to body weight every 4 weeks (maintenance dose) Subcut. injection- 125mg weekly (with or without IV loading dose)	***Order on doctor's request only***
Edarbyclor tablet (Combination product of Azilsartan and Chlorthalidone)	Hypertension	40mg/12.5mg, 40mg/25mg daily	
Enbrel (Etanercept) 50mg pre-filled pen	TNF inhibitor injection for rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis(AS), plaque psoriasis, juvenile idiopathic arthritis and paediatric plaque psoriasis	25mg twice weekly or 50mg weekly subcut. injection	
Lignopad (Lidocaine) 5% medicated plaster	Post-herpetic neuralgia (PHN)	Apply upto12 hours in a 24-hour interval	
Betmiga (Mirabegron) tablet	Overactive bladder (OAB) syndrome	50mg daily	
Aloxi (Palonosetron) 0.075mg injection	Prevention of post-operative nausea and vomiting (PONV)	0.075mg IV injection immediately prior to anaesthesia induction	Aloxi 0.25mg injection for prevention of chemotherapy-induced nausea and vomiting is available in SPH
Tramadol 100mg/ml stada drops	Opioid analgesic for patient with dysphagia	50mg-100mg every 4-6 hours	
Atopiclair cream	Management & relief of itchiness, burning & pain experienced w/ various types of dermatoses	TDS	Atopiclair lotion is already available in SPH
Stratamed gel	Scar treatment	Apply once or twice daily for a minimum treatment of 60-90 days	Can be used on non epithelialised wounds and compromised skin; immediately following surgical procedures, skin resurfacing, trauma, burns and radiation therapy
Xgeva (Denosumab)120mg injection	Bone metastases	120mg subcut. injection once every 4 weeks into thigh, abdomen, or upper arm	Prolia 60mg (Denosumab) injection for osteoporosis given every 6 months is also available in SPH. Please note that the two preparations have different indications
Imojev Japanese Encephalitis vaccine (live, attenuated)	Prophylaxis of Japanese Encephalitis for 12 months of age and over	Single dose of 0.5mL subcut. injection	***Order on doctor's request only***
Eligard (Leuprolide acetate) injection	Prostate cancer	22.5mg subcut. injection every 3 months 45mg subcut. injection every 6 months	Enantone (Leuprolide acetate) 11.25mg 3 months depot injection and 30mg 6 months depot injection are available in SPH. ***Order on doctor's request only***

OUTREACH
ACTIVITIES

外展服務 - 少數族裔人士健康檢查活動

(14/9/2014)

聖保祿醫院於二零一四年九月十四日聯同香港卓護義工協會及聖保祿學校醫療外展服務團隊為香港基督教服務處轄下的「融匯 — 少數族裔人士支援服務中心」提供健康檢查活動，參與的義工和接受檢查服務的少數族裔人士數目多達三百人。義工們包括修女、醫護人員等為眾人提供多種健康檢查活動，包括血壓量度、膽固醇及血糖測試、骨質密度測試、肝/膽/腎超聲波掃描、眼科檢查及牙齒健康講座。

是次活動是本院首次為少數族裔人士提供健康檢查服務，因此別具意義。更重要的是各人均發揮天主教的精神，以愛去關懷和了解被社會忽略的一群。感激各義工的熱心參與和支持，祈盼在不久的將來我們可為更多不同階層的有需要人士提供服務。

INTRODUCTION
OF NEW FACES

Hello everyone, I am Chan Pak To, Eric. It is my greatest pleasure to join this family as a resident rheumatologist. After my graduation, I spent my training in internal medicine and rheumatology. I worked in Tuen Mun Hospital and Pok Oi Hospital before I came to St Paul's Hospital. Upon obtaining my fellowship in rheumatology, I spent most of the time in the Rheumatology Assessment and Treatment Centre of the Pok Oi Hospital, where I carried out rheumatic diseases assessment, treatment and complications screening. The therapeutic armamentarium of rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis has changed significantly since the last decade and now we emphasize on early diagnosis of disease and treatment. The earlier use of biologic therapy to halt radiographic progression is specifically highlighted in different international guidelines. I perform musculoskeletal ultrasound for the early diagnosis of these inflammatory arthritides and guided therapeutic injection. In addition, I deliver biologic therapy to patients with active disease and provide monitoring throughout the treatment course. I look forward to working with all of you and serving patients with different rheumatic diseases.

Dr. Chan Pak To
Specialist in Rheumatology

St. Paul's Doctors Association Golf Tournament

(10/09/2014)

Medical Superintendent Dr. Ho presenting the Four Seasons Trophy to Champion Dr. Tang Yiu Chung