

何鴻燊博士醫療拓展基金會 Dr. Stanley Ho Medical Development Foundation



香港中文大學醫學院 Faculty of Medicine, The Chinese University of Hong Kong

何鴻樂博士醫療稻展基金會醫學新計會 2,0006

Dr. Stanley Ho Medical Development
Foundation Symposium

二零零六年一月七日 7th January 2006

時間 Time:

下午一時三十分至六時 1:30pm-6:00pm

地點 Venue:

澳門旅遊塔會展娛樂中心 四樓會議廳 Grand Hall II, 4/F Macau Tower Convention & Entertainment Centre

統籌主任 Chief Co-ordinator: 胡錦生教授 Professor Kam Sang Woo

香港中文大學 內科及藥物治療學系講座教授 Professor of Medicine and Therapeutics Department of Medicine and Therapeutics The Chinese University of Hong Kong

^{協辦單位 Co-organizer:} 澳門誠興銀行 Seng Heng Bank Limited, Macao

Acknowledgment

In Appreciation

of

Dr. Sai On Chui

Secretary for Social Affairs and Culture

Macao Special Administrative Region

as

Officiating Guest

at the

Dr. Stanley Ho Medical Development Foundation Symposium 2006

7th January 2006

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Message From The Chairman of The Foundation

On behalf of Dr. Stanley Ho Medical Development Foundation, I would like to extend a very warm welcome to you and all participants who attend the "2006 Medical Symposium".

The Symposium marks the first Anniversary of the establishment of the Medical Foundation, and our continued collaboration with the Chinese University of Hong Kong in providing advanced continuation training to medical professionals in Macao Special Administrative Region. Thanks to the efforts of the Chinese University of Hong Kong, a number of renowned medical experts have been invited as keynote speakers, and a lecture program of very high standard has been prepared for the benefit of all participants, including some from adjacent cities in the Mainland.

Macao has experienced spectacular economic and social development in recent years, and an increasing demand for quality medical services is thus inevitable. It is only through continuing professional training, and a program of academic activities and exchanges, that local medical services can be greatly enhanced. The Medical Foundation will continue to take an active role in the development of health-care provision in Macao through its involvement in facilitating professional training and supporting medical research projects.

I take this opportunity to express our gratitude to the organizers who have helped to make this event a success. We also owe our appreciation to medical professionals who have devoted their time and efforts to serving the community of Macao.

We look forward to your continuing guidance and support.

Dr. Stanley Ho

Chairman, Dr. Stanley Ho Medical Development Foundation

Welcome Message

Welcome to the Second Dr. Stanley Ho Medical Development Foundation Symposium jointly organized by the Dr. Stanley Ho Medical Development Foundation and The Chinese University of Hong Kong. Since its inauguration in last January, the Foundation in alliance with The Chinese University of Hong Kong has made great progress in achieving its mission of assisting medical practitioners from Macao in their pursuit of continuing education and life-long training to promote health care standard in Macao and other neighbouring mainland cities. These include update courses and diploma courses in advances in medicine, collaborative interventional research for prevention of environmental smoke-related cardiovascular disease, and outstanding achievement award for health care advances in Macao.

The first exchange symposium held last year focusing on various specialties of internal medicine was a great success. This year the symposium will expand its coverage to include obstetrics and gynaecology, thoracic surgery, orthopaedic surgery and paediatrics. The symposium has received enthusiastic support from leading colleagues of the Faculty of Medicine of our University, and prominent participants from neighbouring Pearl River Delta territories.

We are confident that with your keen participation and interaction, the symposium will be able to deliver the updates and cutting edges in these medical specialties, and enjoy the same success of last year. This symposium will also help to establish a precious and effective platform for further exchanges between medical professionals in Macao, neighbouring mainland territory, and colleagues from the Faculty of Medicine of The Chinese University of Hong Kong.

Professor Jack CY Cheng

Pro-Vice-Chancellor The Chinese University of Hong Kong

Macau Tower Convention and Entertainment Centre (7th January 2006, Saturday)

1:30pm	Registration
2:00pm	Opening Address Presentation & Outstanding Achievement Awards
	Moderators: Professor Jack CY Cheng, Dr. Iek Lap Chan
2:30pm	The Use of NSAIDs in a COX-2 Restricted Environment (by Professor Francis KL Chan, Professor of Medicine, Department of Medicine and Therapeutics, The Chinese University of Hong Kong)
3:00pm	Recent Advances in Prenatal Diagnosis and Therapy (by Professor Tze Kin Lau, Professor, Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong)
3:30pm	Fluoro-navigation in Orthopaedic Trauma Surgery (by Professor Kwok Sui Leung, Professor of Orthopaedics and Traumatology and Chairman, Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong)
4:00pm	Tea Break
~	
	Moderators: Professor Kam Sang Woo, Professor Xu Ming Zhang
4:30pm	Moderators: Professor Kam Sang Woo, Professor Xu Ming Zhang Mini-management of Common Hematological Disease (by Professor Gregory Cheng, Professor, Department of Medicine and Therapeutics, The Chinese University of Hong Kong)
4:30pm 5:00pm	Mini-management of Common Hematological Disease (by Professor Gregory Cheng, Professor, Department of Medicine and
-	Mini-management of Common Hematological Disease (by Professor Gregory Cheng, Professor, Department of Medicine and Therapeutics, The Chinese University of Hong Kong) Bronchoscopic Lung Volume Reduction (by Professor Anthony PC Yim, Professor of Surgery and Chief of Cardiothoracic Surgery, Department of Surgery, The Chinese University of
5:00pm	Mini-management of Common Hematological Disease (by Professor Gregory Cheng, Professor, Department of Medicine and Therapeutics, The Chinese University of Hong Kong) Bronchoscopic Lung Volume Reduction (by Professor Anthony PC Yim, Professor of Surgery and Chief of Cardiothoracic Surgery, Department of Surgery, The Chinese University of Hong Kong) Preterm Infants — Controversies in Management (by Professor Tai Fai Fok, Dean and Professor of Paediatrics, Faculty of



何鴻燊博士醫療拓展基金會 Dr. Stanley Ho Medical Development Foundation

Dr. Stanley Ho Medical Development Foundation

傑出醫療成就獎 2005 Outstanding Achievement Awards

仁伯爵綜合醫院新生兒特別護理病區 (UCERN)的發展和成績回顧 澳門仁伯爵綜合醫院

關於鏡湖醫院微創手術的成果匯報

澳門鏡湖醫院

Review Panel

Professor Anil Tejbhan Ahuja

Professor Lung Wai Chan

Professor Tai Fai Fok

Professor David SC Hui

Professor Rita YT Sung

Professor Kam Sang Woo

Professor Anthony PC Yim



The Use of NSAIDs in a COX-2 Restricted Environment

Professor Francis KL Chan

Department of Medicine and Therapeutics The Chinese University of Hong Kong, Hong Kong

Although current evidence indicates that the cardiovascular (CV) toxicity of cyclooxygenase-2 (COX-2) inhibitors is likely to be a class effect, preliminary data suggest that this adverse event is dose-dependent and occurs only after long-term therapy. It has been postulated that an imbalance in prostacyclin-thromboxane synthesis accounts for the CV toxicity of COX-2 inhibitors. However, a recent epidemiological study found that concomitant low-dose aspirin, which would theoretically restore the prostacyclin-thromboxane imbalance, did not reduce the risk of myocardial infarction among patients receiving high-dose rofecoxib [1]. Interestingly, several observational studies indicated that non-selective NSAIDs also significantly increased the risk of myocardial infarction. Before prescribing anti-inflammatory therapy, one needs to evaluate both gastrointestinal and cardiovascular risk factors of individual patients.

Patients with low CV risk

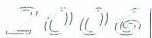
Among patients with low CV risk who require anti-inflammatory analgesics, the management plan can be stratified according to the level of gastrointestinal (GI) risk. Patients without GI risk factors are at low, but not insignificant, risk of NSAID-related ulcer complications. Rational use of NSAIDs is the most cost-effective approach for prevention of ulcer complications in this low-risk category. Elderly patients or those with concurrent major medical illnesses should receive co-therapy with a proton pump inhibitor or misoprostol. Alternatively, celecoxib is as effective as NSAIDs plus a proton pump inhibitor in preventing NSAID-associated ulcer complications [2]. Among patients with multiple risk factors or a history of ulcer complications, neither NSAIDs plus a proton pump inhibitor nor COX-2 inhibitors are adequate for this high-risk category [3]. These patients should avoid using NSAIDs if possible. If regular anti-inflammatory therapy is required for chronic arthritis, the combination of a COX-2 inhibitor and a proton pump inhibitor probably offers the best gastric protection although this approach remains to be examined in prospective trials.

Patients with high CV risk

Patients who have increased CV risk should receive prophylactic low-dose aspirin. Concomitant low-dose aspirin augments the gastrointestinal toxicity of non-selective NSAIDs. Thus, patients taking concomitant NSAIDs and low-dose aspirin should receive a prophylactic proton pump inhibitor. Low-dose aspirin negates the gastric sparing effect of COX-2 inhibitors. Current data suggest that short-term use of celecoxib at low doses (e.g. 100 - 200 mg per day) probably does not increase CV risk. Whether low-dose aspirin will alleviate the CV risk of long-term, high-dose COX-2 inhibitors is unknown.

References

- 1. Levesque LE, Brophy JM, Zhang B. The risk for myocardial infarction with cyclooxygenase-2 inhibitors: a population study of elderly adults. Ann Intern Med 2005;142:481-489.
- Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. New England Journal of Medicine 2002;347:2104-2110.
- Chan FK, Hung LC, Suen, et al. Celecoxib versus diclofenac plus omeprazole in high-risk arthritis patients: Results of a randomized double blind trial. Gastroenterology 2004;127:1038-1043.





Recent Advances in Prenatal Diagnosis and Therapy

Professor Tze Kin Lau

Department of Obstetrics and Gynaecology The Chinese University of Hong Kong, Hong Kong

Over the past few decades, there have been major advances in fetal medicine, in particular on prenatal screening of fetal chromosomal abnormalities, non-invasive prenatal diagnosis, and in utero fetal therapy.

About 0.5% of babies are born with some form of chromosomal abnormalities. Up to date, a definitive prenatal diagnosis of Down syndrome requires the cytogenetic analysis of fetal samples obtained by invasive procedures, most commonly amniocentesis or chorionic villus sampling (CVS). Although a definitive diagnosis is ensured, all invasive tests are associated with a finite risk of procedure-related fetal loss, between 0.5-2%. Therefore, a diagnostic test should only be offered to those who are considered to be at "high-risk" of carrying a baby with Down syndrome. Although maternal age has been used as a simple screening test for decades, its performance is poor with the detection rate (DR) of only 30% at a false positive rate of 5%. Second trimester biochemical screening increases the DR to 60%. However, first trimester combined ultrasound and biochemical screening, which was developed within the last decade, offers the highest DR of over 90%, and enables the screening and detection of abnormal pregnancies at 11-13 weeks of gestation. This effective screening test enables precise estimation of patient-specific individualised risk of carrying an affect baby, and therefore minimises the need for invasive tests (and unnecessary fetal losses due to such invasive tests) with the highest yield.

At the same time, the discovery of cell free fetal DNA within maternal plasma has opened up new horizon in the non-invasive prenatal diagnosis. Although only discovered for about a decade, it is now proven to be reliable and useful tests in the prenatal diagnosis of many genetic diseases. Major advances in the next few years will enable the non-invasive prenatal diagnosis of fetal chromosomal abnormalities. This will further avoid the need of invasive prenatal diagnosis and therefore increase the safety.

With the advances in technology and our understanding in pathophysiology, it is now possible to treat some of the fetal conditions diagnosed in utero, and the most successful examples are fetal anaemia and twin-twin transfusion syndrome (TTTS). Twin-twin transfusion syndrome (TTTS) is a serious complication of monochorionic (MC) twin pregnancies. Without treatment, TTTS is associated with extremely high perinatal mortality of >80%. Traditionally, the only available treatment option for this potentially fatal complication is serial amnioreduction (SA). Although it significantly reduces the incidence of preterm labour and improves the perinatal mortality to 50%, at least 20% of the survivors are neurologically damaged, possibly because of ongoing pathology in the placenta. More recently, fetoscopic laser photocoagulation (FLP) of the placental vascular anastomoses has emerged as the treatment of choice for TTTS. Compared with SA, FLP is a single procedure which is targeted to the underlying pathology. Observational and randomised studies have shown that FLP, compared with SA, has lower perinatal mortality and lower neurological deficit among survivors.

In this lectures, I will summarise the major advances in prenatal diagnosis and fetal therapy over the last 1-2 decades.



Fluoro-navigation in Orthopaedic Trauma Surgery

Professor Kwok Sui Leung

Department of Orthopaedics and Traumatology The Chinese University of Hong Kong, Hong Kong

In orthopaedic trauma surgery, X-ray fluoroscopy is frequently employed to monitor fracture reduction and to guide surgical procedures where implants are inserted to fix the fractures. Fluoro-navigation is the application of real-time navigation on intraoperatively acquired fluoroscopic images to achieve the same goals. The theoretical advantages of fluoro-navigation are:

- Accurate positioning of implants
- 2. Expanding the application of minimally invasive surgery
- 3. Shortening the operation time
- 4. Minimising exposure to X-ray on surgeons, operating room personnels and patients
- Interactive with real-time quantitative assessments

Principles of operation – An interactive image guided computer aided surgery

With the spatial co-ordinates of a standard X-ray fluoroscope and the skeleton, on which the surgical procedures are going to be done, registered into the system, X-ray fluoroscopic images obtained intra-operatively are transferred to the navigation system with automatic scale and distortion corrections. The graphical user interphase then allows the surgeon to navigate with stereostactic tools on the registered biplanar or tri-planar images. As these images are almost the same as those obtained from the standard C-arm, the interpretation of the anatomical features for navigation is simple and straight forward to most surgeons. Surgical procedures can thus be carried out with the virtual fluoroscope.

The technology

Fluoroscopy-based Navigation Systems allows the tracking of a surgical instrument and the superimposing of its contour onto fluoroscopy images. This enables the surgeon to know precisely the position of the surgical instrument at any time of the procedure without the need for taking additional X-ray shots. When an image is taken it is automatically transferred to the navigation system and the position of the image intensifier of the C-arm is localized. Following image distortion correction using metal markers attached to the image intensifier, the image is referenced to the patient's bone which is localized by a further tracker. This allows the removal of the C-arm from the operation field while keeping the registration of the image and visualizing the actual position of the surgical instrument.

For tracking a tool, two basic technologies are available: infra-red based and electromagnetic based. Infra-red technology is very robust and boasts a high localization accuracy, but suffers from line of sight problems. Line of sight problems are not present in the case of electromagnetic systems; however they suffer from distortion problems affecting the accuracy. A new generation of multiple camera based navigation systems using infra-red technologies will combine the advantages of both technologies.

The first generation of tracking devices was characterized by cable based active trackers which suffered from handling limitations. This problem was overcome by the second generation trackers based on passive infra-red reflecting objects. This technology suffered from a limited number of trackable objects and visibility problems when the reflecting surfaces were not clean. The third generation of trackers is based on wireless battery powered active technology and overcomes the limitations of the first two generations. In addition, these trackers are equipped with on-board electronics communicating with the navigation system which allows automatic instrument detection and software remote control.

The applications

Fluoro-navigation is particular important for orthopaedic trauma as the fracture fragments are mobile and the orientations are not fixed before surgery. It is only possible to navigate the images obtained during the operation after fracture reduction or manipulation is completed.

With the development and continuous improvement in the hardware and software, many procedures that require intraoperative fluoroscopic control can now be done with fluoro-navigation. These procedures include:

- 1. Fixation of femoral neck fractures with percutaneous cannulated screws
- 2. Intramedullary locked nails for long bone fractures
- 3. Intramedullary fixation of trochanteric fractures
- 4. Percutaneous fixation of sacro-iliac fractures dislocations
- 5. Percutaneous fixation of iliac wing fractures
- 6. Percutaneous fixation of acetabulum fractures
- 7. Insertion of Ilizarov tension wires for complex articular fractures
- 8. Vertebroplasty and pedicle screw insertion
- 9. Many percutaneous fixation procedures that need fluoroscopic controls

Early clinical experience has confirmed the advantages and the extended applications of this technique will benefit many of our patients. As this is an evolving technology in orthopaedic trauma, more clinical experience are needed for critical analysis.

The future

Further improvement is expected in the system on the hardware and software for quicker image acquisition and accurate registration. More precise positioning and more interactivities will be possible between the system and the surgeons. The development of dedicated surgical instruments for orthopaedic trauma sugary in line with the further improvement of the navigation system will be another major direction. With the establishment of image libraries for instruments, implants and skeleton, further minimising the need for standard X-ray will be possible. The combination of 3-D fluoroscopy and the navigation will improve percutaneous fixation of articular fractures. The possibility to navigate on each individual fracture fragment will extend the technique even more to real-time fracture reduction.

The fluoro-navigation system will also play an important role in surgical training as well as assessment in the virtual surgical environment. This will provide more opportunities for young surgeons to practice and plan surgery. It will open up another frontier in the design for objective assessment of surgical competency.

The unlimited innovation from surgeons on fracture management will definitely expand the application and will popularise the technique in orthopaedic trauma.

References

 Anthony MD III, Branislav J, Bruce DC. Computer Assisted Orthopaedic Surgery – Image Guided and Robotic Assistive Technologies. Clinical Orthopaedics & Related Research 354:8-16, 1998.

- 2. DiGioia AM III, Jaramaz B, Colgan BD. Computer assisted orthopaedic surgery. Image guided and robotic assistive technologies. Clinical Orthopaedics and Related Research 354:8-16, 1998.
- 3. Hinsche AF, Giannoudis PV, Smith RM. Fluoroscopy-based multiplanar image guidance for insertion of sacroiliac screws. Clinical Orthopaedics & Related Research 395:135-44, 2002.
- 4. Hofstetter R, Slomczykowski M, Sati M, Nolte LP. Fluoroscopy as an imaging means for computer-assisted surgical navigation. Computer Aided Surgery 4(2):65-76, 1999.
- 5. Joskowicz L, Milgrom C, Simkiin A, Tockus L, Yaniv Z. FRACAS: a system for computer-aided image-guided long bone fracture surgery. Computer Aided Surgery 3(6):271-88, 1998.
- Kahler DM, Mallik K. Computer Assisted Iliosacral Screw Placement Compared to standard Fluoroscopic technique. Abstract from CAOS/USA '99 p.348.
- Kevin T, David A Simon, Y Raja Rampersaud. Virtual Fluoroscopy: Computer-Assisted Fluoroscopic Navigation. Spine 26(4):347-351, 2001.
- Leung KS. The role of fluoro-navigation in orthopaedic trauma. Lecture presented in Symposium on New Techniques in Fracture Care: Minimally Invasive Surgery and Enhancement of Bone Healing, AAOS 2003.
- Leung KS, Yung SHP, Tsui HF, Tang N, Sarvestani A. 3-D Fluoro-navigation for Articular Fractures A Report of Early Experience. In: Langlotz F, Davis BL and Bauer A: Proceedings of 3rd International Annual Meeting of CAOS: 204-205, 2003.
- Leung KS, Tsui HF, Tang N, Yung SHP, Yue HY. Percutaneous Screw Fixation of Pelvi-acetabular Fractures under Fluoro-Navigation Guidance. In: Langlotz F, Davis BL and Bauer A: Proceedings of 3rd International Annual Meeting of CAOS:208-209, 2003.
- 11. Tsui HF, Griffith JF, Kwok KO, Yung SHP, Leung KS. Accuracy of Three-dimensional Positions of the Sacro-iliac Screws under Fluoro-navigation System. In: Langlotz F, Davis BL and Bauer A: Proceedings of 3rd International Annual Meeting of CAOS:374-375, 2003.
- 12. Leung KS. Fluoro-navigation in Orthopaedic Trauma Osteosynthesis and Trauma Care 12:163-169, 2004.
- 13. Leung KS, Tang N, Yue W. Early Clinical Experience of Gamma-AP Nailing with Fluoro-navigation Osteosynthesis and Trauma Care 13:1-4, 2005.
- 14. Slomczykowski MA, Hofstellter R, Sati M, Krettek C, Nolte LP. Novel computer-assisted fluoroscopy system for intraoperative guidance: feasibility study for distal locking of femoral nails, Journal of Orthopaedic Trauma 15(2):122-31, 2001.
- 15. Starr Adam J, James C Walter, Robert W Harris, Charles M Reinert, Alan L Jones. Technical Tricks Percutaneous Screw Fixation of Fractures of the Iliace Wing and Fracture-dislocations of the Sacro-iliac Joint (OTA Types 61-B2.2 and 61-B2.3 or Young-Burgess "Lateral Compression Type II" Pelvic Fracture. Journal of Orthopaedic Trauma 16(2):116-123, 2002.
- Suhm N. Intraoperative Accuracy Evaluation of Virtual Fluoroscopy A Method for Application in Computer-Assisted Distal Locking. Computer Aided Surgery 6:221-224, 2001.



Mini-management of Common Hematological Disease

Professor Gregory Cheng

Department of Medicine and Therapeutics
The Chinese University of Hong Kong, Hong Kong

Minimally invasive surgery is the current trend in the management of many diseases. Laparoscopic and endoscopic surgeries have less treatment related morbidities and result in shorter hospitalization. To keep up with the fashionable trend and more importantly, because of resources constraints, hematologists also have to take a mini-approach in the management of some common diseases.

ITP

Patients presenting with isolated thrombocytopenia constitute a major portion of in-hospital and outpatient hematological consultations. Most cases (>90%) are due to antibody-mediated destruction of platelets in the spleen (autoimmune thrombocytopenia or ITP).

Mini-approach to the diagnosis of ITP

The diagnosis of ITP is made clinically by exclusion of other causes of thrombocytopenia and is made primarily on the patient's history physical examinations, examination of peripheral blood films. If the above is unremarkable except bruising and thrombocytopenia, the diagnosis of ITP is established and there is no need for bone marrow examination, autoimmune markers etc.

Mini-treatment of ITP

The primary aim of treatment is to maintain a hemostatic platelet count rather than a normal platelet count. The risk of bleeding is minimal when the platelet count is above $30 \times 10^9/1$. For such patient, there is no need for further investigation or treatment.

For platelet counts below 30×10^9 /l, steroid therapy is the first choice. Instead of the traditional high dose prednisolone (1mg/kg) with tapering over 3-6 months, we use a mini-therapy of 4 day-course of dexamethasone. Nearly 40% of patients have a sustained remission after 4 days of treatment.

Mini-warfarin clinic

Many patients are now taking warfarin for various indications and the number keeps increasing. At our hospital, we have been running a mini – warfarin clinic staffed by pharmacists and the control is as good a conventional clinic run by medical officers.

Mini-transplant

Hemopoietic stem transplant is the treatment of choice for many hematological diseases. The traditional myeloablative pre-transplant regimen has substantial treatment related mortalities, and transplant is rarely performed for patients over age 50. Mini-transplant has been shown to have much less toxicities and can benefit the older patients.



Bronchoscopic Lung Volume Reduction

Professor Anthony PC Yim

Department of Surgery The Chinese University of Hong Kong, Hong Kong

Surgical intervention for end stage emphysema includes lung transplantation, lung volume reduction and more recently innovative bronchoscopic approaches. This article will focus on the new nonresectional bronchoscopic approaches to achieve lung volume reduction in patients with end-stage emphysema. It describes the current concepts and strategies that are available today, our clinical experience, and the early results with the use of the one-way endobronchial valve.

Emphysema is a common debilitating respiratory condition due to irreversible airway damage often caused by smoking. For many years, medical therapies have been the mainstream treatment for these patients. More recently, lung volume reduction surgery for patients with end-stage disease has becoming an alternative treatment option (Ciccone et al. J Thorac Cardiovasc Surg 2003;125:513), but patients who need the operation most — those with very low FEV1 and DLCO — are unsuitable for this procedure, as pointed out in recent large scale randomized studies (NETT Research Group, N Eng J Med 2001;345:1075).

Recently, data from clinical studies and animal experiments have indicated that improvements in lung function can be achieved either by plication (Swanson et al. J Am Col Surg 1997;185:25) or by stapling (Brenner et al. Chest 2002;121:201) the most emphysematous tissue without any resection of lung parenchyma, thus suggesting that resection per se may not be necessary. As a result, new concepts have emerged and new devices and strategies developed in order to achieve nonresectional lung volume reduction without the need for invasive surgery. These include creation of extra-anatomical tracts within the major airway (to facilitate expiratory airflow) and induced atelectasis using endobronchial sealants, occluders or valves.

Creation of extra-anatomical tracts

Air trapping and hyperinflation of the lung are commonly seen in emphysematous patients with a resultant increase in the work of breathing together with a sensation of worsening dyspnea. Extra-anatomical tracts can now be created through the bronchoscope between the major airway and the emphysematous lung parenchyma with a radiofrequency probe (Broncus Technologies, Mountain View, CA) using ultrasound guidance. Stents are then put in place in these iatrogenic tracts to prevent them from collapsing (Rendina et al. J Thorac Cardiovas Surg 2003;125:1249). Theoretically, these tracts allow air to be exhaled more readily from the emphysematous lung tissue and can, therefore, facilitate expiration. One of the important potential advantages of this procedure is that it can be used in patients with homogeneous disease — those who are not suitable for LVRS. Evidence from ex-vivo experiment using the diseased lungs removed at the time of transplant surgery with the above approach showed a significant improvement of the FEV1 after creation of these extra-anatomical tracts and the extent of improvement increases with the number of tracts created (Lausberg et al. Ann Thorac Surg 2003;75:393).

Induced atelectasis

An alternative but better-studied concept of nonresectional lung volume reduction is by producing controlled atelectasis in the target areas of the mostly affected portions of the lung, thus achieving lung volume reduction, as well as perhaps allowing redirection of airflow to the healthier portions of the lung. One major advantage of this approach is that it can be done through the bronchoscope and avoids the trauma of major surgery, achieving the clinical benefits of LVRS without the attendant risks.

Several devices and strategies have been developed in an attempt to achieve lung volume reduction in the target segments or lobe(s) through an endoscopic approach based on the above principles, but the majority of these are still in the stage of animal experimentation. Only a few have undergone clinical trials. These devices and strategies take the form of installation of sealants, occluders, and endobronchial valves.

(a) Endobronchial installation of sealants

Animal studies in sheep with bronchoscopic installation of fibrin sealant in the targeted segments to induce absorption at lectasis versus the standard LVRS operation indicated that the nonsurgical treatment was as effective as the surgical group in terms of achieving lung volume reduction with a decrease in the total lung capacity (TLC) and the residual volume (RV) (Ingenito et al. Am J Respir Crit Care Med 2001;164:295). The same group also reported in a separate study in sheep, the use of an alternative agent, a hydrogel scaffolding (3% fibrin containing 0.1% chondroitin-6-sulfacte and 0.1% poly-L-lysine). This material promotes healing and scarring to produce persistent at electasis in the target region without the complications of sterile abscess seen with fibrin glue, but achieving lung volume reduction in 33 out of the 36 target segments (Ingenito et al. Am J Respir Crit Care Med 2003;167:771).

(b) Endobronchial occluders and endobronchial valves

Another approach for bronchoscopic lung volume reduction is to cause isolated lung segments to collapse via endoscopic manipulation of the airways to occlude air entry to these segments.

An early pilot study using either silicone balloons or occluders showed subjective improvement and a reduction in medication requirements for some of these patients (Sabanathan et al. *J Cardiovasc Surg (Torino)* 2003;44:101). However, prosthesis migration and late infection were the main concerns with these early designs. Nonetheless, the results from that study provided some important clues as to the design of the endobronchial device. An ideal endobronchial device should be effective in achieving lung volume reduction; the results should be reproducible; the device should preferably be deployable using a flexible bronchoscope under local anesthesia and should be easily removable bronchoscopically; there should be no prosthesis migration or displacement in the airway; bronchial secretions should be allowed to escape to avoid sputum retention, and the device should not preclude future intervention like LVRS or lung transplantation.

One such device is an umbrella valve designed to allow air to escape on expiration but does not allow inflow during expiration (Spiration Inc., Redmond, WA). An animal study regarding the safety and efficacy of such a device has been presented (Dillard et al. *World Congress of Bronchology* 2002), but clinical data are still lacking up to the time of writing this article.

The most studied device so far in this field is perhaps the one-way endobronchial valve (EBV) (Emphasys Medical Inc., Redwood City, CA) with data now available from both animal (Fann et al.

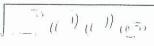
I Bronchology 2003;10:253) and human studies. In a review of the available clinical data (Hwong and Yim. Chest Surg Clin N Am 2003;13:739), it appeared that the results vary widely from the reported series. This might be due to the variations in the patient selection, the exact techniques of endoscopic placement of the EBVs, or the slight variations in the design of the valves. Unilateral insertions of the EBVs were undertaken in one study with significant improvement in carbon dioxide transfer factor and the FEV1 at 1-month follow-up (Toma et al. Lancet 2003;361:931). Another study reported symptomatic improvement in 4 out of 10 patients, with an improvement demonstrated in gas transfer, but without any objective improvement in their exercise tolerance (Snell et al. Chest 2003;124:1073). We reported the result in a prospective cohort study of 20 patients with incapacitating emphysema on maximal medical therapy who underwent EBV placement through rigid bronchoscopy with a 90-day follow-up (Yim et al. J Thorac Cardiovasc Surg 2004;127:1564). Apart from investigating lung function and exercise tolerance as in the two earlier studies, we also analyzed the impact of the procedure on the quality of life of these patients. All our patients survived the procedure, and significant improvements were demonstrated in the spirometric measurements (FEV1) and exercise capacity (6MWD). Furthermore, results of the St. George's Respiratory Questionnaire (SGRQ), the 36-Item Short-Form Health Survey (SF-36) measurements and the degree of dyspnea, measured by the Medical Research Council (MRC) dyspnea grade, improved significantly when compared with the baseline data at 30 days and at 90 days. We have recently reported the combined experience worldwide on the use of EBV and the results are very encouraging (Wan et al. Chest in press).

The procedure appears to be well-tolerated, even in these very high risk patients (some not suitable for surgical LVRS) and, so far, no procedure-related death has been reported. Postoperative complications can occur late after the procedure, with some complications reported to develop weeks after the initial operation. Pneumothoraces remain the commonest complication reported in the clinical trials, occurring as late as 4 weeks after the procedure. From the results of these three studies, it appears that this new strategy of placement of the endobronchial valves is a safe procedure with varying degrees of short-term improvement in the functional status, quality of life, and relief of dyspnea in selected patients with emphysema.

In contrast to the animal experiments, distal bronchial collapse has not been consistently reproduced in the human studies. The lack of radiologic evidence of lung collapse and the absence of persistent spirometric alteration in residual volume (RV) and the total lung capacity (TLC) observed may be related to the presence of significant collateral ventilation within the lungs, as demonstrated by measurements of gas tension of helium (Morrell et al. *Am J Respir Crit Care Med* 1994;150:635). Nonetheless, despite the lack of radiologic collapse, many of these patients showed clinical improvement. The exact reason for this observation is unclear, but may be related to redirection of airflow to healthier portions of the lungs.

Conclusion

The results of nonresectional LVRS, so far, are encouraging. Several strategies and approaches are currently available; however all the investigations are still feasibility studies, and there remain many unanswered questions. New modifications and improvements of the design of the devices will take place and, eventually some will be phased out while others will stay. Optimal patient selection is the key to good outcome. The use of radioactive isotope scan and bronchial blocker to identify those patients with significant collateral flow may be useful in excluding patients who are unlikely to benefit from this approach. This study is currently underway.



The abstracts of Professor Tai Fai Fok and Professor Albert Lee are attached.