Issue 3, June 2007

ANZHSN Bulletin

'New health technologies identified through the Australia and New Zealand Horizon Scanning Network (ANZHSN)'

In This Issue...

Australian Government

Department of Health and Ageing

The role of HealthPACT

This third issue of the Newsletter includes work that has been considered by HealthPACT at the May meeting.

The work of HealthPACT continues to advise the health sector of technologies that are likely to come in the foreseeable future and it is significant that many of the technologies that are now being recommended for adoption onto the Medicare Benefits Schedule were originally identified through the HealthPACT early detection systems. Examples of this include Brain Natriuretic Peptide (BNP) testing where a negative result rules out heart failure and a positive result may suggest heart failure but is not diagnostic of the condition. The impact of such a test is to rule the diagnosis of heart failure out of contention in the assessment of acutely ill patients. Other causes for the patient's shortness of breath, which may not require hospital admission, may then be investigated.

Another new technology is Computed Tomography Coronary Angiography (CTCA) where the value of this new diagnostic test is to exclude significant heart disease and therefore avoidance of people who might otherwise be referred for conventional coronary angiography. Whilst the diagnostic effect of this technologies is obvious, unfortunately we have little valuable information in the Australian health care setting as to those people who currently receive coronary angiography but in whom a CT test would rule out the need. Those patients with a positive CTCA still need to proceed to coronary angiography in order to diagnose more accurately the extent of arteriosclerotic disease in the coronaries to place stents or to prepare for cardiac surgery.

These are challenges that HealthPACT and other health technology agencies will need to master as these technologies become more available and accessible to the Australian community.

CADTH, our Canadian counterpart, also produces a regular high quality Health Technology Update newsletter on new and emerging health care technologies. To sign up for future issues go to https:/secure.cadth.ca/index.phplen/subscribe.

With best regards,
Professor Brendon Kearney
Chair of HealthPACT

Photo courtesy of PDPhoto.org

The use of SMS Text Messages to improve outpatient attendance

Missed appointments are a persistent worldwide problem, with outpatient non-attendance rates between 5 and 42 percent reported in the literature. Similar rates of non-attendance have been documented in Australia. In a recent study conducted at the Royal Children's Hospital in Melbourne, monthly non-attendance rates in an outpatient setting were found to vary between 22 and 28 per cent over a 12-month period[2]. A number of factors have been associated with patient non-attendance. Patients who miss appointments are more likely to be male, of lower socioeconomic status and of a younger age[3]. They are also less likely to own a car and more likely to be unemployed[4]. Non-attendance has also been related to the length of time between referral and appointment, with longer waiting times associated with higher rates of non-attendance[3].

HOW IT WORKS

Short message service (SMS) text messaging is a viable approach for delivering reminders to outpatients. SMS text messaging is cheaper and more efficient than sending a post letter, and less intrusive than a phone call. Mobile phone saturation levels are high in Australia, with an estimated 18 million active mobile services reported as of June 2005[1]. In addition, SMS text messaging allows large batches of individualised text messages to be sent at any one time.

THE EVIDENCE

In a recent trial conducted at the Royal Children's Hospital in Melbourne, SMS reminders were sent to 20,448 patients who had provided a contact mobile phone number and were scheduled to attend an appointment between October and December 2004[5]. SMS reminders were sent to these patients three working days before their scheduled appointment date. Attendance rates in this intervention group were compared to attendance rates in a historical group in which no reminders were issued. The historical group consisted of 18,073 patients who had provided mobile phone numbers and were scheduled to attend an appointment between October and December 2003. Attendance rates were higher in the SMS reminder group for patients attending both new and follow-up appointments. Overall, SMS reminders were associated with a 9.7 per cent increase in attendance rate (90.2% vs. 80.5%, $p < 0.001$). Some questions regarding the validity of results should be raised however given the biases associated with the use of a historical comparison group.

A large randomised trial conducted in Malaysia (n=993) assessed the effectiveness of a program of sending SMS reminders[5]. Patients who received an SMS reminder reported significantly higher attendance rates ($p = 0.005$) compared to those who received no reminder. A cost effectiveness analysis revealed that the cost of sending an SMS per additional attendance gained (A$0.15) was lower than the cost associated with a mobile phone call reminder per additional attendance gained (A$0.29).

FUTURE STEPS

Given the successful implementation of SMS reminders at the Royal Children's Hospital in Melbourne, it is unlikely that any further health technology assessment would be beneficial. Although HealthPACT has recommended that further assessment of this technology is no longer warranted, the contents of this summary should be disseminated to inform all CEOs of major public hospitals of the effectiveness of a systematic reminder programme.

Written by Tom Sullivan, AHTA

Source: stock.xchng (http://www.sxc.hu/photo/778428)

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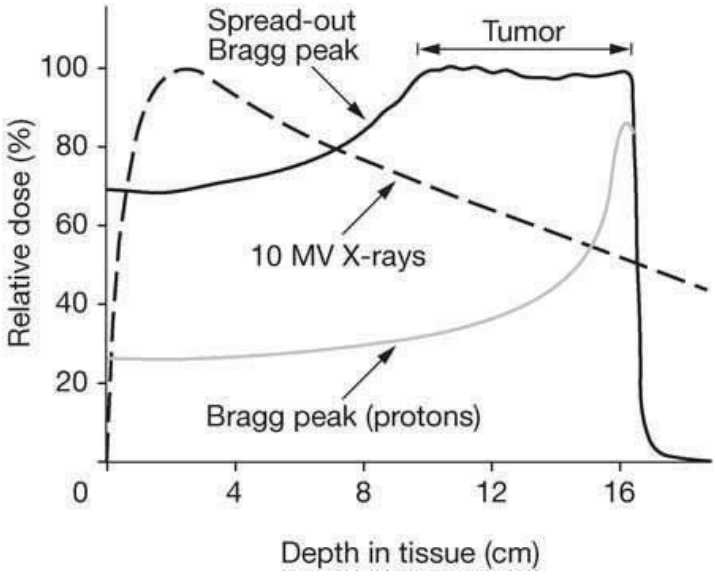
Proton Beam Therapy for the treatment of neoplasms involving (or adjacent to) cranial structures: Executive Summary

Contemporary management of cancers or life-threatening benign tumours often includes a multidisciplinary approach using a combination of surgery, radiotherapy, and chemotherapy specific for the tumour type, histologic grade and the stage of disease. Conventional radiotherapy commonly involves the use of ionising radiation in the form of X-rays or gamma rays (photons), achieving tumour control by inducing DNA damage leading to cell death. However, the dose-distribution of photon radiotherapy leads to the irradiation of healthy tissue adjacent to the target tumour, potentially leading to substantial radiation-induced damage which may result in long-term morbidity or the development secondary tumours. Currently there is a substantially more advanced photon beam delivery method known as intensity-modulated radiation therapy (IMRT) which enables delivery of higher radiation doses to the target tumour while reducing the dose delivered to healthy tissues. However, IMRT may result in an increased volume of healthy tissue irradiated due to the application of numerous radiation fields from different directions.

Proton beam therapy is a form of radiotherapy which is intended to treat tumours in patients where surgical excision is deemed impossible, too dangerous or unsuccessful. The key advantage of protons compared to photons is its superior dose-distribution profile (see Figure 1). Protons have a rapid energy loss in the last few millimetres of penetration, which results in a sharply localised peak dose known as the Bragg peak. By modulating the penetration depth of the protons it is possible to target the Bragg peak precisely to the target tumour while sparing the healthy tissue beyond the tumour from radiation. This could prove to be useful in neoplasms involving, or adjacent to, cranial structures due to the proximity of the tumour(s) to critical structures. The proton beam procedure involves the construction of detailed treatment plans with the aid of 3D PET or CT scans to ensure the accurate delivery of the proton beam. The treatment plan is constructed with input from clinicians, medical physicists and dosimetrists, which will determine the precise angle, proton beam energy (to determine penetration) and the dose per treatment for each individual patient.



Left: Depth dose distribution in tissue of a single Bragg peak (grey), a spread-out Bragg peak (black), which consists of multiple Bragg peaks of different energy added together, and a 10 MV X-ray beam (dashed)

(Yock & Tarbell (2004), 'Technology Insight: proton beam radiotherapy fro treatment in pediatric brain tumors', Nature Clinical Practice Oncology, 1, 97-103).

To date, treatment-planning studies have concluded that proton beam therapy results in substantial dose-sparing to adjacent critical structures which may translate to lower toxicity and thus increased survival. Unfortunately, clinical studies have not consistently proven that *proton beam therapy* is significantly better compared to *conventional photon therapy*. The prevalence of proton radiation-induced side effects in the studies included in this assessment appears to be within the range expected for conventional photon therapy, with some studies inferring that proton therapy is substantially safer. However the lack of consistency across studies and the lack of direct comparative studies severely limit the conclusiveness of these results. Meanwhile, most included studies reported local tumour control rates which are similar to conventional photon radiotherapy as well.

It has been estimated that the construction of a two-gantry proton facility would cost approximately $100 million; in comparison construction of an X-ray facility would cost $28 million. Operational costs per fraction were estimated to be $1,700 for proton therapy and $700 for X-ray/photon therapy. It is likely that proton beam therapy will continue to be substantially more expensive compared to conventional photon therapy despite accounting for future cost reductions. Other studies reported that the average cost per QALY gained for the treatment of left-sided breast cancer, prostate cancer, head and neck cancer and childhood medulloblastoma with proton therapy was $17,000. However these calculations were

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Proton Beam Therapy for the treatment of uveal melanoma: Executive Summary

Uveal melanoma is the most common primary intraocular malignant tumour with an incidence of 6 to 7 cases per 100,000 population. In Australia, 233 new cases of ocular cancers were reported in 2001; however, unlike other cancers (e.g. skin melanoma), the incidence of malignant ocular tumours is projected to remain relatively stable. Before the development of modern eye conserving treatment modalities, identification of uveal melanomas was usually followed with enucleation (removal of the eye). However, with the development of new techniques, current treatment is aimed at conserving the eye with useful vision whenever possible. Radiotherapy has gained substantial popularity as one of the main treatment modalities for uveal melanoma (brachytherapy and external beam therapy), however one of the key difficulties in utilising radiotherapy is confining the radiation dose to the target tumour.

The features of proton beam therapy discussed previously may make it an attractive modality for the treatment of uveal melanomas, where sensitive structures (fovea, optic disc etc.) are often located in close proximity to the tumour. Patients undergoing proton beam therapy are required to undergo a surgical procedure to suture tantalum clips onto the sclera around the tumour base to identify the tumour margins. In addition to this, a 3D model of the patient's eye is constructed with a treatment planning program in order to precisely identify the location of the tumour and to ensure than the proton beam is targeted accurately.

Studies have reported that numerous complications can occur when treating uveal melanomas with both radiotherapy, and proton beam therapy. These complications include rubeosis, neovascular glaucoma, cataract and vision loss. Overall, studies have shown that patients treated with proton beam therapy for uveal melanoma experience significant complications. However, due to the lack of comparative studies and the large variation between existing proton beam therapy studies, no firm conclusions can be made on the relationship of proton beam therapy and these ocular complications. Most of the studies included in this assessment report that proton beam therapy is capable of achieving good tumour control rates (~ 95%) and patient survival rates are comparable to brachytherapy. In one comparative study, enucleation rates appear to be higher for proton beam therapy patients compared to patients treated with ^{125}I and ^{106}Ru brachytherapy; however this study was flawed due to the varying pre-treatment characteristics in each patient group. It should be noted that studies on proton beam therapy for the treatment of uveal melanomas varied substantially with regards to patient characteristics, tumour size, treatment margins and total apical radiation dose. Therefore, comparisons across studies are often difficult and the lack of high-quality evidence prevents the elucidation of the advantages of proton beam therapy compared to other existing radiotherapy techniques.

In conclusion, the evidence on the safety and effectiveness of proton beam therapy for the treatment of uveal melanomas is mixed. The local tumour control rates achieved are remarkably consistent across studies despite the heterogeneity across study cohorts and methodology, and at the very least appears to be comparable to brachytherapy. In addition, the incidence of metastasis and overall patient survival is comparable to brachytherapy as well. However, it is unclear if proton beam therapy results in a substantial improvement of eye preservation rates and the ocular complications observed post-treatment are of concern. Further studies are required to address the flaws of previous studies and to compare proton beam therapy to existing techniques.

Written By Irving Lee, ASERNIP-S

Proton Beam Therapy for the treatment of neoplasms involving (or adjacent to) cranial structures: Executive Summary

(Continued from page 3)

attained utilising various assumptions which dilutes its conclusiveness and hence should be interpreted with caution.

In conclusion, the evidence for proton beam therapy in neoplasms involving, or adjacent to, cranial structures remains inconclusive. Further studies are required to determine if proton therapy is indeed substantially better compared to conventional radiotherapy, as inferred by numerous treatment-planning studies.

Written By Irving Lee, ASERNIP-S

Fermiscan: The detection of breast cancer through the analysis of diffraction patterns of human hair

The TGA have taken the view that Fermiscan is developing *a service* not a product. Fermiscan is not considered to be a medical device as no medical device is employed either in the sampling of human hair or in the production of a diffraction pattern. Therefore Fermiscan is not considered a therapeutic good and the regulatory requirements for advertising therapeutic goods do not apply. This technology was evaluated as it may be *"associated with obvious safety and ethical issues or controversies."*

HOW IT WORKS

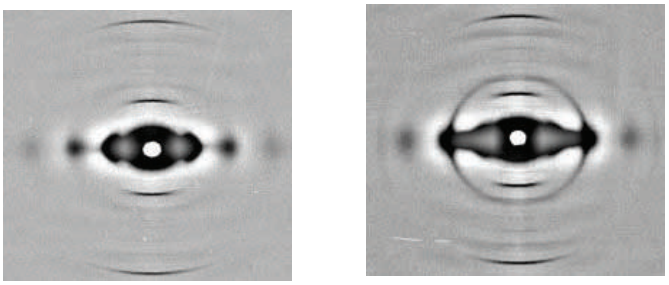
Bone morphogenetic proteins (BMPs) are involved in controlling a number of biological functions. BMPs have been studied in cancer, especially breast cancer, with variable results. Fermiscan relies on the same BMPs being expressed in hair as in breast cancer.

It is hoped that differences in the molecular structure of hair will be observed in individuals who have breast cancer. The molecular structure of hair can be determined using X-ray diffraction generated by a synchrotron[1,2].

THE EVIDENCE

The diagnosis of breast cancer by studying the diffraction patterns of human hair was first reported by James et al in 1999. Blinded synchrotron analysis was conducted in the United States. The resultant small angle X-ray scatter (SAXS) patterns were analysed and the breast cancer status of the samples were determined (see Figure). Of the 23 hair samples taken from women diagnosed with breast cancer, all (100%) returned a positive SAXS image for breast cancer. Of the women *not* diagnosed with breast cancer, 24/28 (86%) returned a SAXS image that was normal. No follow-up information was made available on the 4/28 women who were found to have a positive SAXS image for breast cancer. Five high-risk women (familial history of presence of BRCA1 mutation) were analysed and 3/5 (60%) returned a positive SAXS image indicating the presence of breast cancer [4].

A number of studies attempted to replicate the results of this initial study without success. A double blind study on the diffraction hair patterns of 109 women was conducted: normal population (n=27), unaffected by breast cancer and



(a) (b)

Above: Hair diffraction pattern of patient without breast cancer (a) and with breast cancer (b) (James et al 1999)

are BRCA1 or BRCA2 negative (n=23), unaffected and are either BRCA1 or BRCA2 positive (n=10), known to have breast cancer and are BRCA1 or BRCA2 negative (n=21), known to have breast cancer and are BRCA1 or BRCA2 negative (n=25), and no family history (n=3). A positive SAXS image was returned in 15/27 (56%) of the normal population, 15/23 (65%) of the unaffected (BRCA1/2 negative) and in 7/10 (70%) of the unaffected (BRCA1/2 positive) women. Of those women with breast cancer, there were 10/21 (48%) positive samples for those BRCA1/2 negative and 7/25 (28%) positive for those BRCA1/2 positive. The authors concluded that there is no measurable association between the diffraction patterns observed and breast cancer [5]. James has attributed the failings of these studies to poor sample preparation and analysis [6, 7].

A total of 500 hair samples have been analysed using this technique in a number of small studies [8]. No false negatives were reported, however a number of false positives were, and these results would have implications for the women involved in terms of follow-up procedures.

An Australian validation trial is currently being conducted by Fermiscan Ltd in conjunction with a number of private radiology clinics. The trial will involve Australian women who have been referred to radiologists by their GP for a mammogram. These women will then be asked if they would like to participate in the Fermiscan® trial. Fermiscan Ltd aim to enrol 2,000 women in this trial and results will be unblinded in stages once the first 200 samples are analysed [3].

FUTURE STEPS

It appears that this technique is not reproducible in the hands of a non-specialist. Sample preparation is the key to

producing consistent and correct results and research groups other than Professor James do not appear able to replicate these ideal conditions, limiting the applicability of this technology as a diagnostic tool. There is limited and conflicting data available, and a lack of reported follow-up on false positive samples. However, it is likely that there would be a high demand for a non-invasive breast cancer diagnostic technique from women of all ages.

HealthPACT has recommended that further assessment of this technology is no longer warranted. However, in light of ethical concerns and the potential to do harm, HealthPACT have recommended that this summary be disseminated to the National Breast Cancer Centre and consumer groups.

Written by Linda Mundy, AHTA

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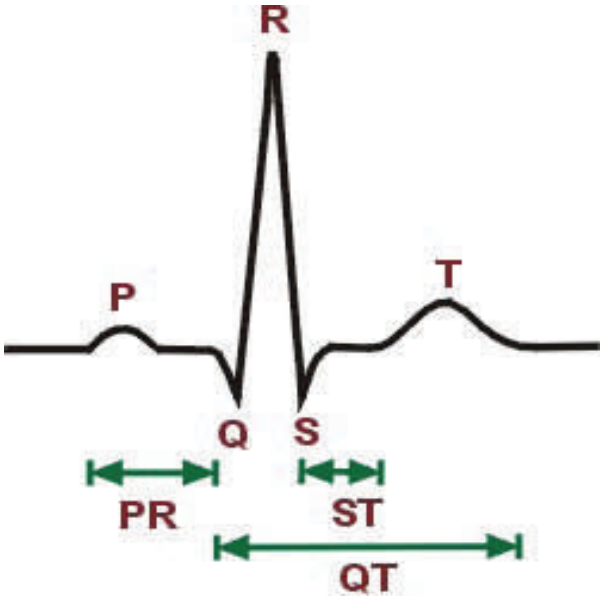
Genetic testing for congenital long QT syndrome: Executive Summary

Congenital long QT syndrome (LQTS) is caused by mutations in a set of genes (LQT 1-8) which code for protein subunits of cardiac ion channels. The main clinical feature of LQTS is the elongation of the QT interval on electrocardiograms (ECGs). The majority of LQTS patients are asymptomatic and are diagnosed either by family history or by virtue of having survived an episode of syncope or severe ventricular arrhythmia. Unfortunately, for many LQTS patients, the first presentation of symptoms is sudden cardiac death, usually occurring in healthy children or young adults.

It is estimated that LQTS affects approximately 1: 5,000 individuals in the United States and that it would be reasonable to expect that this prevalence would hold true in Australia and New Zealand. Research has suggested that a number of deaths in young people that have previously been ascribed to causes such as drowning, motor vehicle accidents and sudden infant death syndrome may be attributable to LQTS.

LQTS is usually diagnosed using clinical indicators; including past episodes of syncope with or without stress; congenital deafness, length of QTc obtained via ECG; torsade de pointes; T-wave alternans; notched T wave in 3 leads; low heart rate for age; and family history all combine to give a patient an overall clinical score. Based on this score patients are rated on their probability of having LQTS. Mutational analysis of LQTS involves the use of polymerase chain reaction (PCR) with products then analysed using either single-strand conformational polymorphism or denaturing high performance liquid chromatography and, if required, subsequent DNA sequencing. DNA is usually obtained and isolated from a blood sample but also may be obtained via a mouth swab.

Molecular diagnosis is intended to identify asymptomatic family members of identified LQTS probands who have not been identified via clinical screening and may be at risk of sudden death. In addition, individuals deemed to have an intermediate or high risk of LQTS according to the diagnostic criteria of unexplained syncope, a prolonged QTc on an ECG or a family history of sudden cardiac death would be candidates for screening by mutational analysis. Approximately 30-35 per cent of questionable cases of LQTS will *not* be picked up by molecular diagnosis due to the large number of mutations implicated in LQTS and the possibility of a large number of as yet unidentified mutations.



Above: A normal ECG

(Klabunde, R. E. (2005). Cardiovascular Physiology Concepts [Internet]. Available from: http://www.cvphysiology.com/Arrhythmias/A009.htm

The only safety outcome reported by papers included for assessment in this report was the high number of genotype negative individuals, as the lack of identification of a genetic defect does not rule out the presence of LQTS.

Clinical assessment alone may not be sufficient to detect silent gene carriers who are asymptomatic for LQTS but are at risk of experiencing life-threatening cardiac events. One study reported a high number of asymptomatic carriers (21.4%) in family members of probands, underlining the importance of DNA analysis for individuals with an ambiguous clinical diagnosis. A high quality study directly compared the results of molecular analysis to the results of ECG (QTc) and the Schwartz Clinical Score in family members of probands. There was a low penetrance (25%), indicating that although a high number of family members were genotype positive (72%), the majority of these were clinically asymptomatic. When compared to mutational analysis, ECG and clinical score both had a low sensitivity (38%) but 100 per cent specificity. This study therefore demonstrates that molecular analysis is superior to clinical diagnostic techniques for the identification of "silent" LQTS carriers when a known mutation is screened for in family members.

In studies of *unrelated* patients, conflicting results were reported with one study finding a good correlation with clinical criteria and the corrected QT interval and LQTS diagnosis, as both of these factors were statistically significant in the genotype positive group ($p < 0.0001$). However, this was contradicted in another smaller study, which reported that 32 per cent of the tested population were negative for a LQTS mutation despite the fact that 81 per cent of these individuals had clinical symptoms of LQTS and the mean QTc of this group was elevated at 484 ± 46 ms.

A follow-up of this study reported on targeted mutational analysis for the rare LQT4 on patients previously found to be genotype negative for the more common mutations (LQT1-3 and LQT5-6). This study demonstrated the value in a *fully* comprehensive initial mutational analysis, as a further nine patients (3.3%) previously thought to be LQTS negative were found to be positive for this rare mutation.

A cost-effectiveness analysis of genetic testing for familial LQTS in *symptomatic index cases* was conducted. The expected cost-effectiveness of genetic testing of *first-degree relatives* or more distant relatives was not included in this analysis. The three most common mutations were examined in the KCNQ1, KCNH2 and the SCN5A genes. Genetic testing of probands was found to be cost-effective compared to no genetic testing, at a cost per year life saved of US$2,500, well below the standard threshold of US$50,000 per life-year saved often used to define a cost-effective intervention. A further cost-effectiveness analysis is required to consider the benefits of genetic testing of family members of the proband.

In conclusion, clinical symptoms and an elongated QTc may not necessarily predict LQT and a negative mutation analysis may not rule out a diagnosis of LQTS. Studies included in this assessment reported that mutational analysis appears to be superior in the diagnosis of LQTS carriers when compared to clinical assessment alone. In addition, once a proband has been identified, targeted screening of family members for a specific mutation may be a cost-effective measure for extended family screening. Mutational analysis of suspected LQTS patients appears to be effective in identifying individuals previously thought to be clinically asymptomatic, and this may have long term consequences for their future. As the first symptom of LQTS for many patients is a life-threatening cardiac event, early diagnosis is of utmost importance.

Written By Linda Mundy, AHTA

Intraoperative ultrasonography to achieve negative margins without the need for guide wire during surgical excision of breast cancer

Ultrasonography has many diagnostic and therapeutic applications which are widely used in medicine. Intraoperative ultrasonography to guide breast cancer excision appears to be a recent new application of the technology. Clinical studies suggest this new application of ultrasonography may lead to improved resection margins as well as offer further advantages to the surgeon and hospital.

HOW IT WORKS

Intraoperative ultrasonography for breast cancer surgery is a less traumatic technique for tumour localisation without the need for the use of a guide wire. The technique was first described in 1988 and can be carried out by either a radiologist or appropriately trained surgeon in the operating room[1]. This method of visualisation is unique as it allows for visualisation of the tumour during the excision procedure at all times[2]. Its use has the potential to not only reduce patient pain and anxiety but also make breast cancer surgery faster and more efficient as the requirement for use of equipment in the radiology department is no longer required. The technique can lead to the immediate assessment of margin status of the excised lesion and potentially reduce the number of re-excision resulting from positive margins[3]. Not all lesions can be visualised with ultrasound, including micro-calcifications or speculations extending a distance from the tumour mass[4] .

THE EVIDENCE

A randomised clinical trial compared margin clearance and lumpectomy size with ultrasonography-guided breast cancer excision (n=26) versus the gold standard (n=23) (wire-guided breast cancer excision)[2]. One patient randomised to wire-guided excision suffered displacement of the wire and underwent ultrasonographic guided excision. Immediately following excision, the resected specimens were checked by the radiologist in the operating room using ultrasonography. Ultrasound-guided excision performed significantly better than guide-wire excision in terms of the achievement of adequate cancer-free margins (i.e. ≥ 1 mm). Adequate margins of ≥ 1 mm was achieved in 24/27 patients (89%) who received ultrasonography compared to only 12/22 patients (55%) in the guide-wire group (p = 0.007). Margins of < 1 mm (close margins) were achieved in 2 (7%) ultrasonography patients and 6 (27%) guide-wire patients (no significance test reported). Only one patient in the ultrasonography group attained focally positive margins compared to four in the guide wire group (no significance test reported).

In an earlier report Moore and colleagues published their results evaluating the efficacy of intraoperative ultrasound in obtaining adequate surgical margins in women undergoing lumpectomy for breast cancer (Moore et al. 2001). Unlike the report by Rahusen et al. (2002) the women included in this study all had palpable breast cancer.

An earlier RCT of women with palpable breast cancer (n=51) reported only one ultrasonography patient presented with a positive margin, compared to seven patients (29%) in the control group ($p < 0.05$)[5]. All patients, with the exception of one control patient who presented with positive margins underwent re-excision or mastectomy. Additionally the margin of uninvolved breast tissue was greater in the ultrasonography group (7.6 ± 2.0 mm) compared to the control group (4.8 ± 1.4 mm).

FUTURE STEPS

Intraoperative ultrasonography to guide excision of breast cancers is not a new technique. At the time of writing it is unclear if intraoperative ultrasonography during breast cancer surgery is a technique regularly used by breast surgeons in Australia. The data presented have demonstrated promising results in achieving negative margins and potential advantages for patient, surgeon and hospital. Given the potential benefits to be gained through the widespread use of this technique it is recommended that a Horizon Scanning Report is conducted.

Written by Luis Zamora, ASERNIP-S

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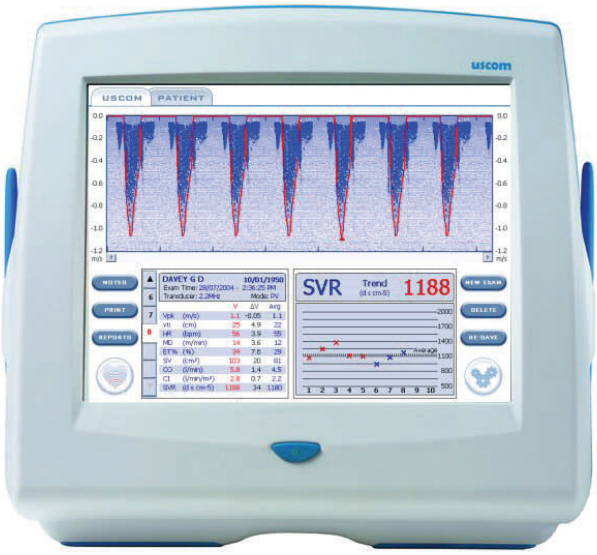
USCOM: Ultrasound cardiac output monitor for patients requiring haemodynamic monitoring: Executive Summary

The USCOM device is a non-invasive, ultrasound cardiac output monitor designed to measure and record changes in the haemodynamic status of critically ill patients transcutaneously. The USCOM utilises continuous-wave Doppler ultrasound and can measure both left and right cardiac output.

Cardiac output (CO) is the key variable in the assessment of haemodynamics especially in the management of critically ill, or peri-operative patients or patients undergoing anaesthesia. The USCOM device may be used to confirm normal cardiac function, detect and quantify abnormal function, and to evaluate the effectiveness of cardiovascular therapies.

In the intensive care and operating room setting, the "gold standard" method used to assess CO is bolus thermodilution using the standard pulmonary artery catheter (PAC). Although this technique is widely disseminated there is no evidence that it facilitates patient recovery or improves survival. Other methods for measuring CO include minimally invasive methods such as the Fick re-breathing method, dilution techniques using isotonic lithium chloride, the insertion of a trans-oesophageal Doppler transducer and pulse contour analysis of the aortic waveform. A truly non-invasive method for measuring CO is the thoracic electrical bioimpedance method.



Above: The USCOM monitor (printed with permission USCOM Pty Ltd)

There were no adverse events associated with the use of the USCOM device reported by any of the studies included for assessment.

Inter-assessor agreement between CO as measured by medical staff undergoing training with the USCOM device, compared to values obtained by trained clinicians was good (r= 0.91). Three studies found that trainees were able to rapidly acquire the skills necessary to produce reliable CO measurements in ED patients. In addition, two case series reported on the time required to use the USCOM device to obtain a CO measurement at the scene of an emergency, prior to, or during patient transportation to hospital. Average time spent ranged from 15-25 seconds and did not contribute to extended times at the scene or transportation time.

Cross classification studies, comparing CO levels obtained with USCOM to those obtained with the "gold standard" PAC reported either a non-significant bias between the two techniques (-0.14 to 0.18) or a significant correlation (r = 0.794, $p< 0.01$). That is, there was no systematic difference between the 2 measures of CO. Small limits of agreement (including 0), indicated that there was little difference in the 2 methods of measurement. These results were supported by 2 of the 3 abstracts which compared USCOM to measurements taken with PAC (r= 0.80, r^2 = 0.714), however one study reported a large bias (-1.04 ± 1.29 L/min) compared to the mean CO of 5.3 ± 0.57 L/min. Two studies reported that when CO values exceeded 5 L/min, the values obtained with the USCOM tended to *underestimate* CO. This may suggest that the USCOM device may adequately measure CO values within the normal physiological range, however further validation studies for low and high CO states should be conducted. In addition, 2 studies found that clinicians were unable to obtain a successful Doppler signal at *both* the ascending aorta and the pulmonary artery, however a successful signal was able to be obtained from at *least* one of these locations.

There are currently no cost-effectiveness data available for the utilisation of the USCOM device for CO monitoring. The USCOM unit is currently selling in Australia for $35-42,000 and after the initial purchase of the unit (monitor and probe) there are no recurring costs apart from standard ultrasound conducting gel.

In conclusion, the USCOM device appears to be safe and effective for the measurement of cardiac output in critically ill patients. Further studies in patients in high and low cardiac output states may be recommended.

Written By Linda Mundy, AHTA

Sentinel lymph node biopsy for colorectal cancer to detect nodal metastases

Conventional histopathology techniques for examining lymph nodes in patients with colorectal cancer appear to be inadequate. Approximately 30% of node-negative patients die as a result of recurrence or metastases. The use of sentinel node mapping to stage colorectal cancer may increase the detection of nodal metastases, lowing recurrence rates.

HOW IT WORKS

Sentinel node identification involves injecting a tracer to map the lymphatic drainage pathway from the tumour. The most common technique uses a combination of blue dye and radioisotope, although good results have been reported with single modality techniques [1]. In patients with colorectal cancer, the blue dye and/or radioisotope is injected into the subserosal surface of the bowel immediately adjacent to the base of the tumour. After several minutes, the mesentery is visually inspected to determine the location of sentinel nodes, which are characterised by the uptake of blue dye. If radioisotope was injected, a gamma counter is also used to pinpoint the nodes. All sentinel lymph nodes (SLNs) are marked with sutures or clips and are later removed and examined by a pathologist to determine if nodal metastasis is evident [2].

THE EVIDENCE

A systematic literature search identified 17 case series studies on SLN mapping for colorectal cancer: 15 describing SLN mapping with blue dye alone and 2 describing SLN mapping with a combination of blue dye and radioisotope [3]. Most of the included studies performed microscopic examination of SLNs using multisectioning, H&E-staining and/or immunohistochemical staining.

Ten studies using blue dye alone reported identification rates from 90-100%, while the remaining 5 studies reported rates from 71-87%. In 3 studies that used a laparoscopic method, the identification rate was 100%. Accuracy ranged from 78-100%. The false-negative rate varied substantially across the included studies, ranging from 0-54%. Possible upstaging percentages were between 3-20%, while the percentage for true upstaging (increase in patient's identified cancer stage e.g. from stage II to III) varied between 0-6% [3].

Of the two studies that used a combination of blue dye and radioisotope for SLN mapping, one employed an *ex vivo* technique. This achieved an identification rate of 88%, a sensitivity of 55% and a 45% false-negative rate. It is noteworthy that only 51% of blue nodes were radioactive, while 81% of radioactive nodes were dyed blue. The two remaining studies that utilised an *in vivo* technique achieved an identification rate of 98%. One study utilised ultrastaging techniques, with a sensitivity and false-negative rate of 83% and 17%, respectively. A true upstaging rate of 19% was revealed after immunohistochemistry (IHC) analysis of the SLNs. The use of radioisotope identified an additional 10 SLNs (5%), but only one of these SLNs would not have been identified with the use of blue dye alone. The addition of radioisotope tracer for SLN mapping did not appear to provide any substantial improvement in identification rates compared to blue dye alone.

Overall, the accuracy rates for SLN mapping ranged from 93-100%, with sensitivity rates of between 90-100% and true upstaging rates of 5-14%. However, the prognostic significance of IHC- and/or RT-PCR-detected micrometastases remains unclear. Only 25% (3/12 studies that reported on micrometastases) of the included studies reported that the detection of micrometastases correlated with significantly worse survival rates [3].

FUTURE STEPS

While the evidence for SLN mapping in patients with colorectal cancer suggests it may reduce the risk of understaging, compared to conventional techniques, it is still an experimental procedure. The large variation in results among studies reflects the lack of a standardised technique and a universal definition of which stained lymph node(s) should be considered SLNs. In addition, the true value of SLN mapping for improving nodal staging in colorectal cancer will only be demonstrated if it translates into improved survival for patients with accurately staged colon cancer. Based on the evidence currently available and the potential impact of this technique, HealthPACT recommended that this technology be monitored for further information in 12-months time.

Written by Irving Lee, ASERNIP-S

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Other New and Emerging Technologies

The following additional technologies were considered by the Health Policy Advisory Council on Technology (HealthPACT) in May 2007.

- Excimer laser-assisted nonocclusive anastomosis (ELANA) for extracranial-to-intracranial and intracranial-to-extracranial bypass, primarily for treating giant aneurysms of the intracranial circulation and cerebral atherosclerosis
- Photoselective vaporisation for benign prostatic hyperplasia
- SprayGel adhesion barrier system for the prevention of adhesion formation following ovarian surgery
- Vacuum assisted closure for enterocutaneous fistulas
- Radiofrequency assisted liver resection for patients with liver tumours requiring hepatectomy
- Intrabronchial valve for chronic obstructive pulmonary disease

The above technologies can be accessed on the following link:

http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/asernip-s-net-s-summaries-2

- GeneSearch™ Breast Lymph Node (BLN) Assay for women undergoing sentinel lymph node biopsy for breast cancer
- Delayed enhancement MRI for detection of myocardial viability
- Screening for Chlamydia in pharmacies
- Perinatal Hepatitis C Screening
- MRI guided high intensity focused ultrasound for non-invasive treatment of symptomatic uterine fibroids
- EasyOne™ Spirometer for the diagnosis and management of chronic respiratory disease and asthma

The above technologies can be accessed on the following link:

http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/prioritising-summaries-2006-2

PRODUCTION NOTES

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