

# SIR-SPHERE TRIAL IN METASTATIC COLORECTAL CANCER

FEBRUARY/MARCH 2008

by Dr Gavin Marx

With 12,500 new cases diagnosed yearly, colorectal cancer is the second most common cancer in Australia. The primary disease is readily resectable, resulting in an extended survival duration, however the outlook for survival is clouded by the occurrence of metastatic lesions. During the course of their disease roughly half of all colorectal cancer patients will present with or will acquire hepatic tumours. Appearance of the disease in the liver is historically indicative of end stage disease, with long-term survivors being rare.

For those with liver only metastases, the first option is resection or radio frequency ablation, with both of these techniques having curative potential. With an improvement in surgical technique and chemotherapy options 5 year survivors are seen in 30-50% of cases. These techniques are however limited to just 10-15% of patients. Treatment options for the vast majority of patients are confined to chemotherapy. With the addition of Oxaliplatin, Irinotecan, Capecitabine and some novel biologic agents such as Bevacizumab (Avastin) and Cetuximab significant improvements in progression free and overall survival rates are now being seen. Unlike other cancer forms such as breast cancer, head and neck cancer or cervical cancer, the use of radiation as a treatment moiety is not viable as the normal liver is prone to radiation damage at sub-therapeutic activity. On this basis the chemo-radiation combination successfully producing sustained disease free intervals in solid tumour types elsewhere in the body cannot be replicated in the liver.

For those patients with unresectable disease in the liver, the gold standard chemotherapeutic regimen in the first line setting is known as FOLFOX (folinic acid, 5-fluorouracil, oxaliplatin). Typically 50 – 60% of patients will respond to this treatment and the median progression free survival is 8 – 9 months. Following progression of the disease treatment is typically continued with an Irinotecan based regimen and in some cases biological agents, yielding an overall survival from the time of diagnosis of the metastatic disease of more than 20 months.

The liver has a dual blood supply, with the hepatic arterial blood supply delivering 15% of the blood to the liver and the portal vein delivering 85% of the blood to the liver. Hepatic lesions are metabolically active thus they parasitise the oxygen rich arterial blood supply, drawing 95% of their blood supply from the arterial vasculature, with less than 5% coming from the portal supply. SIR-Spheres microspheres (Sirtex Medical Limited) utilise this dual hepatic blood supply to target the tumour while sparing the normal liver parenchyma. Radio-labelled microspheres are implanted via a femorally inserted hepatic arterial catheter, concentrating in the tumour rim and delivering a lethal level of radiation to the tumours, while sparing the normal liver parenchyma.

The microspheres, which are smaller than a human hair, use the radioisotope Yttrium-90 which is a pure beta emitter with a half life of 64.1 hours and a mean penetration distance in tissue of just 2.5 mm. Millions of these microspheres are implanted as part of this procedure, lodging permanently within the liver. Unlike chemotherapy that is administered on a fortnightly basis, this procedure is carried out once only with the implantation being carried out by a specially trained expert at the San. This involves a multidisciplinary approach with oncology, nuclear medicine and interventional radiology. This process has been used in the past for patients having relapsed post chemotherapy.

An international randomised controlled trial is currently underway, evaluating the impact of SIR-Spheres administered with first line chemotherapy. This study is underway at the San. It is aimed at assessing the impact of targeted radiation plus FOLFOX chemotherapy as a treatment option for patients with liver predominant metastatic colorectal cancer. It is hoped that this combination treatment will see an increase in response rate from 50-60% to 70-80% with a corresponding increase in the progression free survival rate. The study is open to recruitment for the next fifteen months.

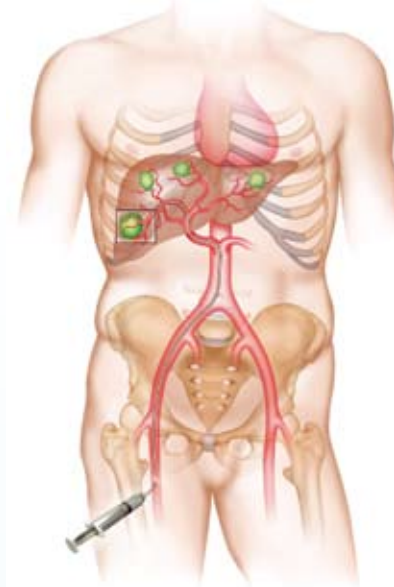


Figure 1. Overview of the microsphere administration procedure.



Figure 2. Injected microspheres targeting the tumour vasculature.



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# INFLAMMATORY BREAST CONDITIONS

by Dr Meagan Brennan

Inflammatory lesions of the breast are common and are frequently related to lactation (mastitis and breast abscess.) There are, however, other inflammatory conditions such as granulomatous mastitis and inflammatory breast cancer that are often more difficult to diagnose but must be recognised as their treatment and clinical course are vastly different to that of infective conditions.

Inflammatory symptoms should be investigated as other breast symptoms are with imaging (mammography and/or ultrasound depending on age and clinical findings) followed by fine needle biopsy or core biopsy of any significant clinical or imaging abnormalities.<sup>1</sup>

Inflammatory breast cancer may masquerade as mastitis. It is therefore important that suspected infective conditions be followed to complete clinical and imaging resolution. Where an infective lesion does not resolve or does not behave as expected, the diagnosis of inflammatory breast cancer should be considered.

## MASTITIS AND BREAST ABSCESS

Lactational mastitis usually presents within the first few weeks of breast feeding, with pain, erythema, swelling, lump(s) and fever. The causative organism is most frequently *Staphylococcus aureus* and treatment is with oral antibiotics (flucloxacillin, dicloxacillin or cephalexin 500mg qid) for at least ten days. Courses shorter than ten days carry a risk of incomplete treatment and subsequent relapse. In some cases intravenous treatment may be required. Careful attention to attachment and positioning during breast feeding also forms an important part of management.

Abscess may develop and should be suspected when there is increasing pain with a firm, localised, discrete lump which is associated with intense tenderness and erythema. If abscess is suspected, ultrasound examination should be performed. Abscess has traditionally been treated by surgical incision and drainage but usually this can be avoided by performing serial percutaneous aspiration, often under ultrasound

guidance, and antibiotic therapy that may need to be continued for several weeks. Women with mastitis and abscess may continue to breast feed and should be advised that the infection and antibiotics do not harm the baby.

Mastitis may also develop independently of lactation. It may be caused by cysts that become infected or may occur spontaneously. Mastitis unrelated to lactation must be investigated fully with imaging and often biopsy, and followed to complete resolution to ensure that it is benign.

Periductal mastitis is an inflammatory condition that presents with nipple redness and discharge. It occurs in young women, and is associated with smoking in 90% of cases.<sup>2</sup> Recurrent episodes of periductal mastitis are common and are often slow to respond to antibiotic treatment. Surgical excision of the large ducts around the nipple may be required although surgery is often complicated by poor wound healing.

## GRANULOMATOUS MASTITIS

This is a rare cause of inflammation in the breast. It is a benign condition that is often characterised by a chronic relapsing course. It is usually diagnosed on biopsy when a presumed case of bacterial mastitis does not respond to antibiotic treatment. The aetiology is unknown; there has been some recent discussion about a possible association with *Corynebacterium*.<sup>3</sup> Treatment with prednisone and methotrexate have variable success. Surgical management is also an option but is also associated with a risk of recurrence.

## INFLAMMATORY BREAST CANCER

Inflammatory cancer is a specific clinical presentation of breast cancer and it should be considered in the differential diagnoses of every inflammatory breast condition. Inflammatory carcinoma represents 1-4% of breast cancers, and has a particularly poor prognosis.<sup>4</sup> The classic presentation is one of rapid onset of an ill-defined breast mass, pain, breast enlargement, erythema and peau d'orange. An inflammatory presentation of breast cancer does not imply a particular histological type but this

presentation is associated with aggressive tumours, often with gross axillary lymph node involvement at presentation. Breast imaging may reveal very little, showing only subtle changes of increase in skin thickness and increase in tissue density rather than the classic features of breast cancer such as a spiculated lesion with microcalcification. A multidisciplinary approach to management is essential as treatment often initially consists of a coordinated regimen of chemotherapy and radiotherapy. Surgery (usually mastectomy and axillary clearance) is frequently reserved for later in the treatment program and in some cases may not be recommended at all.<sup>1</sup>

## REFERENCES

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- 4 Parker LM, Boyages J, Eberlein TJ. Inflammatory carcinoma of the breast. In: Harris JR, Hellman S, Henderson IC, Kinne DW, editors. Breast diseases. Philadelphia: JB Lippincott, 1992;775-82.



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# SPLENECTOMY AS A LAPAROSCOPIC PROCEDURE

by Dr Trevor Currer

The introduction of Minimal Access Surgery to all surgical disciplines has been one of the most important developments in modern medicine. Laparoscopy, a form of Minimal Access Surgery, has been the greatest advance in abdominal and pelvic surgery for decades. Cholecystectomy, the flagship of laparoscopic abdominal surgery, has benefited millions of people, worldwide, since 1990.

Anecdotally, I recall attending a lecture, given in 1992, by Alfred Cushieri, regarded as the father of laparoscopic surgery in Britain and Europe. He predicted "that every abdominal operation could potentially be performed laparoscopically and hence that laparoscopic surgery may have no boundaries".

This may be true.

However, to what benefit of the patient?

Only a relatively few laparoscopic procedures have survived scientific scrutiny, showing a proven benefit over the "open" procedures. In addition to cholecystectomy, these include the following procedures:

- anti-reflux and hiatal hernia surgery.
- diagnostic and "staging" laparoscopies in malignancy, together with palliative bypass procedures.
- inguinal hernia surgery in men, in particular for bilateral or recurrent hernias.
- bariatric surgery.
- splenectomy and adrenalectomy.
- benign colorectal disease and more recently Colon cancer. (Rectal cancer unproven).
- retroperitoneal dissection (suitable in the lower abdomen and pelvis only).
- appendicectomy (unproven benefit over "Minimal Access Open Surgery").

Since the early days of laparoscopic

abdominal surgery, splenectomy was regarded as a natural progression for the laparoscopic surgeon. The only limitation has been the relatively few medical indications for this procedure. The spleen lends itself to laparoscopic removal because of its "end" organ vascular status, easy accessibility, and its well defined anatomical attachments.

Since the first laparoscopic splenectomy, reported by De Laitre, in 1991, several technical developments have facilitated this operation:

1. Positioning: in the semi-lateral position (60 degrees to horizontal) is preferable, with a "broken" operating table. This exposes the spleen perfectly, and allows adjacent structures to "fall away" and opens the space between the lower costal margin and the iliac crest.
2. Ultrasonic dissector: allows control of the short gastric vessels and division of the lienorenal splenocolic, splenogastric and lienophrenic ligaments.
3. Articulating endovascular stapler: suitable for vascular control of the splenic artery and vein.
4. Extraction bag: following division of all attachments, the spleen is inserted laparoscopically into an extra large Endocatch extraction bag, which prevents spillage of splenic tissue thereby obviating the formation of splenic "rests". The spleen is removed via a 12mm port site after morcellation within the extraction bag.

The past three decades have seen major changes in the treatment of splenic disorders. These changes were partly based on the scientific evidence indicating that splenectomy renders the patient at lifelong risk for increased susceptibility to infection. The most serious of these infections is the overwhelming post splenectomy infection (OPSI) which occurs

in 0.5% of trauma patients and with an incidence of 10 to 20% of patients who have haematological diseases. The mortality associated with OPSI is between 50% and 70%. Sepsis as a cause of death is 200 times more prevalent in the splenectomised patient than in the general population.

Splenectomy is performed with several possible intentions:

The treatment of primary and secondary hypersplenism, and for diagnostic and staging purposes in primary haematologic diseases. Primary hypersplenism may be caused by any of the three types of congenital red cell disorders associated with haemolytic anaemias: membrane disorders; haemoglobinopathies; and erythrocyte enzyme deficiencies. Secondary hypersplenism may be associated with myelo- and lymphoproliferative disorders and with portal hypertension.

The commonest indication for splenectomy is ITP where the spleen itself is intrinsically normal and surgery is performed to

prevent thrombocytopenia associated with antibody-laden platelets sequestering in the spleen.

Other conditions which may require splenectomy include splenic infarcts, cysts, tumours, splenic artery aneurysm, sarcoidosis, Gaucher's disease, and pancytopenia in Felty's syndrome. Benign cysts and tumours may be suitable for partial splenectomy, which can now be safely performed laparoscopically. With regard to splenic injury in trauma patients, "conservation" remains the mainstay of therapy. In the event of surgery being required, spleen-preserving procedures are performed, and this remains within the domain of "open" surgery.

The laparoscopic procedure is the "gold standard" for splenectomy in 2008 supported by substantial scientific medical evidence accrued during the past sixteen years.

## NEWLY ACCREDITED DOCTORS.

The SAH Board of Directors has recently approved the following doctors to be added to our list of Accredited Medical Officers:

- Dr Mandy Baillie – Radiology
- Dr Mastaneh Daghighi – General Practice
- Dr Lynne Dowd – Surgical Assistant
- Dr Annie Ho – Radiation Oncology
- Dr Lewis Holford – Anaesthesia
- Dr Hagop Kiyork – Orthopaedic Surgery
- Dr Samuel Kuo – Surgical Assistant
- Dr George Lau – Cardiology
- Dr David Lee – Surgical Assistant
- Dr Matthew Lilley – Anaesthesia

## SAN DAY SURGERY HORNSBY

- Dr Amarjit Sandhu – Anaesthesia

## NEWS FROM THE SAN

### FREE CANCER SUPPORT GROUPS

Cancer Support at the San holds a number of support groups for patients with bowel, lung, breast and prostate cancer or melanoma. It also holds a stoma group and carers group. For more information doctors and patients can contact group facilitator Nerolie Gate on 94879061.

### HITH - HOSPITAL IN THE HOME

The San's Hospital in the Home (HITH) program allows patients access to the San's medical and nursing services in the privacy and comfort of their own home. Patients are treated at home before being discharged back to their general practitioner. For queries call HITH Medical Director, Dr Suhan Baskar on 9487 9111.

### PATHOLOGY SERVICES - DID YOU KNOW?

San Pathology offers a comprehensive range of pathology services including electro-cardiography (ECG) testing along with home visit and doctor's office courier services. The home visit service caters for patients who are unable to visit collection centres and extends to residential aged care homes and retirement villages.

### CHILDREN'S SLEEP DISORDERS UNIT

The San's purpose built Children's Sleep Disorders Unit has 4 overnight stay rooms and operates 4 nights per week. Parents stay with the children. Dr Hugh Allen and Dr Chris Seton can refer children for assessment to assist in diagnosis of a range of sleep disorders including sleep disordered breathing, sleep parasomnias, restless leg syndrome, and other behavioural issues. Space/castle/marine/airplane decorated rooms and themed fairy/super hero/teddy nights make the stay a fun adventure. Contact Manager Kate Mulvan on 9487 9347.

### 2008 SAN GP CONFERENCES

Welcome to the new RACGP Triennium 2008 - 2010.

The first San GP Conference for the year will be "Plastics" offered by San Day Surgery Hornsby on Tuesday April 29th 2008. Invitations will be sent in MArch. A complete list of San GP Conferences for 2008 will be listed shortly on [www.sah.org.au](http://www.sah.org.au) under "Events".



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# MARCH 2008

1	Saturday	Red Cross Calling Month
2	Sunday	Clean up Australia Day
3	Monday	
4	Tuesday	
5	Wednesday	
6	Thursday	
7	Friday	
8	Saturday	International Women's Day
9	Sunday	
10	Monday	10-14 National Orthoptic Awareness Week
11	Tuesday	
12	Wednesday	
13	Thursday	13-15 World's Greatest Shave
14	Friday	Bandaged Bear Day
15	Saturday	13-20 Coeliac Awareness Week
16	Sunday	
17	Monday	17-23 Brain Awareness Week
18	Tuesday	
19	Wednesday	National Youth Tobacco Free Day
20	Thursday	
21	Friday	
22	Saturday	
23	Sunday	
24	Monday	World Tuberculosis Day
25	Tuesday	
26	Wednesday	
27	Thursday	
28	Friday	
29	Saturday	
30	Sunday	
31	Monday	

### PAYING BILLS ON SAH WEBSITE

A new function to allow patients to pay their bills on line is now ready. To access this function go to [www.sah.org.au](http://www.sah.org.au)