

## Next Generation Photodynamic Therapy (PDT) and Sonodynamic Therapy (SDT)

### Role of Treatment in Cancer

Photodynamic therapy is the use of light sensitive substances, which accumulate selectively in cancer cells and when exposed to light of an appropriate wavelength causes an excited state, which is able to transfer its energy to oxygen. This transfer of energy causes the electrons in oxygen to rearrange and assume a different electronic configuration, where all electrons in the oxygen molecule have paired up, resulting in a particular electron spin configuration. This is highly reactive and initiates a series of events that leads to the release of Cytochrome C from the mitochondria (these are the engines of the cell and are present in large numbers in all cells) and this initiates tumour cell death. Tumours tend to be hypoxic (lacking in oxygen), so in treatment protocols in some cases, we use ozone auto-haemotherapy, which is a method of increasing oxygen at the tumour site.

Sonodynamic Therapy is the use of low-level ultrasound and this produces tumour destruction from the non-thermal effects of ultra sound, especially cavitations in malignant cells. Ultra sonic cavitations generate free radicals from the breakdown of water molecules. The Photodynamic agent we use is also sensitive to ultrasound frequencies. This approach allows deeper penetration into the body. Sonodynamic therapy is carried out using a simple therapeutic ultrasound machine with an especially designed treatment head known as a maniple, which is applied over the affected area with some ultrasound gel placed on the skin. This is done after the light bed exposure; (see 'A review of research into the uses of low level ultra sound in cancer therapy', Uyu Wang & Mason in Ultra Sonics Sonochemistry, Vol 11, issue 2, April 2004, pages 95 — 130).

Most photo-sensitizers come from a class of naturally occurring compounds called porphorins. Natural porphorins are breakdown products from recycled haemoglobin and are inherently light sensitive. These accumulate in tumours and cause cancer cells to auto-fluoresce.

PDT has several advantages over surgery and radiotherapy: it is comparatively non-invasive, it can be targeted accurately and repeated doses can be given without the total dose limitations associated with radiotherapy, and the healing process results in little or no scarring. PDT can always be done on an out-patient/day case setting as the treatment has no side effects. Possible side effects occur due to tumour breakdown, these are as follows:

1. Tiredness – feeling exhausted which can be treated symptomatically and is quite commonly observed.
2. Discomfort or pain around the tumour site due to inflammation.

3. Occasional mild bruising over tumour site is sometimes observed on the skin following PDT.
4. **If the tumour is attached to a blood vessel, bleeding can occur during treatment because of tumour breakdown. If it is attached to a major blood vessel the consequences can be life threatening**

No photosensitivity from normal ambient light, artificial or natural, has been noted with the use of Sonalux. **As a precaution however**, we advise you to not go out in direct sun light for periods of over half an hour for 1 week following administration of Sonalux.

In prostate cancer, there is a small risk of incontinence and impotence. This has not been noted in any case of prostate cancer treated with this method so far. However, it is noted significantly when fibre optics are inserted into the prostate and PDT is given in this manner. This is not the method we use.

The next generation of Photodynamic Therapy is a significant advance on previous PDT. This uses a specific agent which does not have to be given intravenously and can be given orally. It accumulates selectively in tumour sites and it does not persist in the skin. It is also a whole body treatment, and it does not require the use of lasers. The agent is sensitised by a specialised light bed consisting of several tens of thousands of light emitting diodes, emitting in the red light region and the infra-red region of the spectrum. The treatment programme can be repeated as often as is necessary, and for advanced tumours it is best to treat slowly so as to avoid too rapid a tumour break down in too short a time.

## Method of Treatment Using Next Generation Photodynamic Therapy

The patient is assessed clinically. Then the agent is taken orally, with the drops being absorbed under the tongue. 48-72 hours then elapse whilst the agent clears from the skin and accumulates selectively in tumour sites. Following this the patient is exposed on the light bed to appropriate light frequencies from light emitting diodes. The time of exposure is important and can vary from 5 minutes up to 15 minutes for patients with less advanced tumours, to only a few minutes for patients with more advanced tumours (the more advanced the tumour, the slower the treatment programme). Exposure on the light bed initially occurs consecutively on three days following the 48-72 hours after administration of the oral agent.

Further light bed exposure is then calculated on an on-going clinical basis. The patient is given enough oral agent to cover one treatment cycle.

Anecdotally there has been the best success using Next Generation PDT with breast cancer and prostate cancer. Ultrasound is then administered over the tumour area.

We often combine ozone auto-haemotherapy with PDT. PDT relies on the production of singlet oxygen ( $O$ ). This is derived from oxygen ( $O_2$ ). Tumours are characteristically hypoxic (showing low oxygen levels). Ozone auto-haemotherapy is an effective way of increasing oxygenation just before light bed exposure, therefore increasing the effectiveness of the PDT.

**OUTCOMES OF OUR FIRST 115 CASES**  
**USING PHOTODYNAMIC/SONODYNAMIC THERAPY**  
**(PDT/SDT)**  
**FROM 2005**

## **INTRODUCTION**

We use a bacteriochlorin agent which is sensitive to red light (616 nanometres) and ultrasound. We have animal studies using the mouse sarcoma 180 model, showing significant tumour destruction from red light and ultrasound (in the case of ultrasound, experiments were done in complete darkness using ultrasound only) and this demonstrated that the agent is sensitive to ultrasound and to red light (616 nanometres).

Where there is significant tumour mass, we have to control the inflammatory response which occurs following PDT. Practically all tumours swell initially if the PDT has been successful, due to a release of large concentrations of pro inflammatory cytokines. The most effective way of controlling this is to use Dexamethasone at a varying dose depending on the severity of the symptoms post PDT in each particular patient.

We have begun to fractionate treatments, as a result of our clinical experience with patients with significant tumour mass.

Judging results from photodynamic therapy, can be challenging as when initially the tumour swells, the tumour could, initially, look bigger on scanning. Because private scans are relatively expensive, doing scans before and after each course of PDT is not an every day option for us. Therefore, we tried to look at biochemistry pre and post PDT. We have looked at tumour markers, relevant to the particular patient being treated and also tumour marker 2 Pyruvate Kinase and cell free DNA. We have compared these to controls of the same tests in patients with stable cancer. Broadly speaking, if we get a significant change in any of these readings pre and post PDT, this corresponds clinically to a useful response. In those patients with no significant change before and after, generally there has not been a significant response to the PDT.

The vast majority of our patients are late stage cancer patients. All post surgery chemotherapy and radiotherapy.

The form of PDT used was well tolerated.

Treatment - the main disadvantage is that where there is significant tumour load, a marked release of pro-inflammatory cytokines occurs and the resulting inflammatory response has, in some cases, to be controlled by the use of Dexamethasone, in a varying dose depending on the specific clinical situation.

We carried out, in as many cases as possible, pre and post PDT, standard bloods, cell free DNA, tumour marker 2 Pyruvate Kinase and an appropriate tumour marker, depending on the case. The laboratories measuring cell free DNA and Pyruvate Kinase have, in each case, one specific biochemist dealing with these tests. When this biochemist was away on holiday, or where one of the periods when patients were having PDT coincided with public holidays such as Christmas, Bank Holidays, in these situations the blood tests could not be done.

We also looked at using Telomerase but found that the results obtained differed wildly both in the control subjects and in the PDT patients, so this was found not to be a useful measure.

We did control tumour marker 2 Pyruvate Kinase, cell free DNA and standard tumour markers in a range of stable cancer patients. We are currently having these results statistically evaluated. When this has been done we will put in the P value (probability value) for each case.

### **Tumour Marker 2 Pyruvate Kinase**

Cell proliferation is a process that consumes large amounts of energy. A key sensor for this regulation is the glycolytic enzyme, Pyruvate Kinase, which determines whether glucose carbons are channelled to synthetic processes or used for glycolytic energy production. The mammalian tumour marker 2 Pyruvate Kinase isoenzyme, can switch between a less active dimeric form and a highly active tetrameric form which regulates the channelling of glucose carbons either to synthetic processes (dimeric form) or to glycolytic energy production (tetrameric form). Tumour cells are usually characterised by a high amount of the dimeric form leading to a strong accumulation of all glycolytic phosphometabolites above Pyruvate Kinase. Therefore, this looks at glycolytic activity in the body. Tumours tend to be glycolytic.

Essentially, what we have found in our observational study is that Pyruvate Kinase may go up or down in any particular patient but this usually corresponds to a clinically useful response. In other words, there isn't a clear direction as to whether it goes up or down post PDT.

### **Standard Tumour Markers**

Standard tumour markers, such as CA 125 (ovary), CA (oesophagus, lung, bile duct, pancreas, bladder, colon) CA 19.9, (oesophagus, bile duct, pancreas), CA 15.3 (breast) and prostate specific antigen (prostate), tend to go up post PDT but this is not always the case. We find that a significant change up or in some cases down post PDT as compared to pre PDT correlates with a clinical response.

## **Cell Free DNA**

The term 'Free-DNA' is widely used, but Cell-Free DNA is more correct. Most of the non-related DNA in blood plasma is likely to be down to protein molecules (2). Hence, before measuring Cell-Free DNA it is appropriate to use a reagent that uses a proteinase to assist in freeing DNA that is bound to proteins (3). Most circulating DNA has been released from degrading cells and is mainly present as nucleosomal elements from the enzymatic chopping-up of the genomic DNA (4). In healthy people the circulating Cell-Free DNA is at a very low level (2, 5). The top end of normal is 9 units. Higher concentrations are found in malignancy (6 – 11). Autoimmune disorders (4), severe infections (12, 14). Burns and traumatic injuries can also show high levels of Cell-Free DNA. In other words increases are associated with significant disease (15).

## **The Use of Ozone Autohaemotherapy Together With PDT**

We found significantly better results by using ozone autohaemotherapy before each light bed treatment with PDT. Tumour hypoxia is often marked, and during PDT oxygen is consumed as shown in Sitnik et al's (16) paper on the reduction of tumour oxygenation during and after photodynamic therapy.

## **Immune Response**

There is increasing evidence that killing tumour cells using photodynamic therapy resulting in tumour cell necrosis, increases expression of tumour antigen. This should lead to more effective anti-tumour vaccines. It is impossible to say at this early stage whether increased expression of tumour antigen leads to antigen specific T cell responses (17).

## **Tumour Cell Necrosis**

Method of cell death in PDT is by tumour cell necrosis; this as pointed out above produces a marked increase in pro-inflammatory cytokines with an accompanying marked inflammatory response. This can last for several weeks. The use of Dexamethasone, in particular is especially useful in terms of controlling this reaction.

This is a list of all 115 patients we have seen using PDT/SDT from 2005. There were few cases lost to follow-up.

The median survival times were suggested by the patient's Oncologist.

The ages stated are the patient's age at the time of treatment.

The overall conclusion from this list is that repeating PDT/SDT on many of these patients, following the first treatment course, would definitely produce a treatment advantage; the time interval between the courses being judged on a clinical basis. Those patients with large tumour mass have to be treated carefully under steroid cover and in some cases the treatment course needs to be fractionated. This is because tumour cell death with PDT/SDT happens rapidly and is always followed by an inflammatory response due to tumour cell necrosis. Combining PDT/SDT with chemotherapy has been found to give a better tumour cell destruction than with chemotherapy alone.

The issue of tumour recurrence remains of significance in metastatic cancer, for any method of tumour cell destruction, be it chemotherapy, radiotherapy or Photodynamic/Sonodynamic Therapy.

Photodynamic/Sonodynamic Therapy is clearly an effective treatment as it does not have the downside of chemotherapy and radiotherapy and is therefore a realistic option for these patients following failure of conventional treatment approaches. Using sonodynamic therapy has enabled us to penetrate bone.

The majority of patients coming for Photodynamic/Sonodynamic Therapy were reluctant to spend funds on regular scans, therefore before and after PET CT scans, the ideal method of scanning pre and post PDT/SDT, was not available for these patients, as they preferred to spend their funds on the treatment process.

	<b>Male/Female</b>	<b>Age</b>	<b>BLADDER CANCER</b>
1	Male	50	This patient came to see me in December 2007. He had a transitional cell carcinoma of the bladder, blocking the right ureter, producing a right hydronephrosis. From a conventional point of view, radical surgery (cystectomy) was the recommended course of action, but he flatly turned this down partly because his wife is chronically ill and he has to look after her and such an operation would involve him being in hospital for several week. We did PDT/SDT on him during February 2008 and he coped with this well. When I last saw him in February 2009, he had not had an operation, the blockage to the right ureter had resolved and he has been passing bits of necrotic tumour. Median survival time unknown.
2	Female	69	This patient came to see me in February 2008. She had transitional cell carcinoma of the bladder with a secondary in the left scapula. The scapula secondary became clinically obvious in late 2007. The bladder cancer was diagnosed in July 2006. She had surgery to the bladder (not a cystectomy) in November 2006. When I saw her she had recurrence in the left scapula and also in the bladder. Her median survival when I saw her was 6 months. We carried out PDT/SDT with Dexamethasone cover, 2 milligrams twice daily. The scapula secondary became more painful initially due to the local inflammatory response, but on examining it 3 months post-PDT it had decreased in size by 50%. She developed bladder symptoms and these appeared as stones in the bladder (calciums attracted to cancer cells) and she was clearly passing some necrotic tumour from the bladder. This patient died in February 2009.

### **BRAIN TUMOURS**

3	Female	50	This patient came to see me in April 2008 with a massive ependymoma; she had had surgical debulking and radiotherapy. Her tumour was diagnosed in 2003. She had been offered Temozolomide but did not wish to take this up. We did PDT/SDT on her in April 2008. When I first saw her her clinical state was poor and her median survival time was 6 months. We carried this out under Dexamethasone cover, 2 milligrams twice daily.
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			A month after PDT/SDT she went on a 2 month safari with her husband to Africa. She has remained relatively symptom free and we did another 2 week course of PDT/SDT in October 2008. Repeat scans shows that the tumour has decreased in size, the scans were done in December 2008. I last saw her in February 2009. She is well and symptom free.
4	Male	56	This patient presented in September 2005 with a left temporal lobe glioblastoma multiforme. This patient had a median survival time of 2 months when I saw him. The tumour was recurrent following a partial resection in January 2005. We carried out PDT/SDT on him in November 2005. This patient died in January 2006.
5	Male	66	This patient presented to us in March 2005 with a glioblastoma multiforme in the left temporal area, which was diagnosed in January 2005. He had had whole-brain radiotherapy at the end of March 2005. We carried out PDT/SDT on him in August 2005. At the time of treatment his median survival time was 3 months. He died in December 2006.

## **BREAST CANCER**

6	Female	41	This patient presented in July 2005 with metastatic breast cancer with multiple bony metastases. Her median survival time was 18 months. It was an oestrogen positive tumour, but she refused Tamoxifen. We carried out PDT/SDT on her in August 2005. This patient died in December 2008.
7	Female	41	This patient presented in July 2005 with a right-sided intraductal breast cancer; oestrogen receptor negative, HER2 negative. She was offered neo-adjuvant chemotherapy, then a lumpectomy with a sentinel node biopsy and possible radiotherapy post-surgery. She refused neo-adjuvant chemotherapy and radiotherapy, but decided on neo-adjuvant PDT/SDT. This was carried out in August 2005. She had a lumpectomy and the tumour consisted of necrotic tissue with no active tumour seen. The sentinel node biopsy was clear of tumour. At the time of writing (February 2009), she is recurrence free.
8	Female	67	This patient presented in September 2005. In 2002 she developed a Grade 3 left-sided breast cancer, oestrogen negative and HER2 negative. She had a right sided mastectomy in 2002. She then developed DCIS in May 2003 and had chemotherapy for this which was helpful. In 2003

			she had a prosthesis put into the left breast and this prosthesis was removed in July 2005. She presented with a large tumour in the right breast (recurrent). In the left breast she had a wide area of granulation tissue where the left sided prosthesis had been removed. The was an 'open area'. We carried out PDT/SDT in September 2005. Her median survival when I saw her was one year. We know this patient survived at least 2 years, but since that time she has been lost to contact.
9	Female	52	This patient presented to us in August 2005, with multiple bony secondaries from breast cancer. We carried out PDT/SDT in August 2005. During the PDT/SDT the pain in the hip and back disappeared. The pain then returned, but nothing like as bad as it had been previously. This patient's median survival time when I saw her was 2 years. This patient died in November 2008.
10	Female	49	This patient presented in October 2005 with widespread metastatic breast cancer. We did PDT/SDT on her in October 2005. At that time her median survival was 3 months. She died at the end of February 2006.
11	Female	51	Presented in June 2005 with widespread metastatic breast cancer, extending over both breasts and around the back of the chest. We did PDT/SDT on her in October 2005. This patient has been lost to follow up.
12	Female	55	Presented with metastatic breast cancer with bony metastases in November 2005. Her median survival time at that point was 2 months. We carried out PDT/SDT on her in November 2005. She died on 24 December 2005.
13	Female	56	Presented in December 2005 with metastatic breast cancer, with several bony metastases and also a lung secondary. Her median survival time at the time of seeing her was 6 months. We carried out PDT/SDT on her in January 2006. This patient died in August 2006.
14	Female	53	Presented with metastatic breast cancer in March 2006, with several bony metastases. We carried out PDT/SDT on her in April 2006. Her median survival time on first seeing her was 2 years. At the time of writing (Feb 2009), she has stable disease.
15	Female	51	Presented in March 2006 with breast cancer, with multiple bone metastases. We carried out PDT/SDT on her in April 2006. Her median survival time when I saw this patient was one year. The pain in the bony metastases increased during the PDT/SDT and this pain settled some 4-6 weeks after post-PDT. This patient died in November 2006, having developed brain metastases.
16	Female	30	Presented in October 2005, with widespread metastatic breast cancer with bone metastases and liver metastases.

			Her median survival time at the time of her first appointment was 3 months. We carried out PDT/SDT on her in January 2006. This patient has been lost to follow up.
17	Female	57	Presented in June 2006 with a metastatic breast cancer with multiple bone metastases and also metastases in the liver and a cutaneous metastases on the right side of the chest and also brain metastases. Her median survival time when I saw her was 3 months. We carried out PDT/SDT on her in July 2006. This patient died in December 2006.
18	Female	50	Presented in Sept 2006, with left sided breast cancer, diagnosed in August 2004. She refused any conventional treatment and had been treating herself with alternative therapies ever since her diagnosis. She came requesting PDT/SDT. She refused a bone scan or a CT scan. Her median survival time when I saw her was one year. We carried out PDT/SDT on her in Sept 2006. Post-PDT/SDT the tumour in the breast increased in size due to an inflammatory reaction and this gradually settled over a period of 3-4 months. Patient died in July 2008.
19	Female	67	Presented with metastatic breast cancer in September 2006, with widespread bony metastases and several liver metastases. When I saw her in September 2006 her median survival time was 3 months. We carried out PDT/SDT on her in September 2006, under Dexamethasone cover (2 milligrams twice daily). There was increased pain in the bony metastases post-PDT/SDT but this settled down some 6 weeks following PDT/SDT. This patient died in February 2007.
20	Female	41	Presented in September 2006, with a recurrent breast cancer in the scar following a lumpectomy, which was carried out in 2001. Post PDT/SDT the recurrence contracted down to two-thirds of the size it was previous to PDT/SDT. Median survival time at the time of first seeing her was unknown. This patient has been lost to follow up.
21	Female	53	Presented in October 2006 with metastatic breast cancer, with several bony metastases. We carried out PDT/SDT on her in November 2006 and for a month following that, the bone metastases were more painful. We carried out the PDT/SDT under Dexamethasone cover (2 milligrams twice a day). Her median survival time at the time of first seeing her was 2 years. At the time of writing she has stable disease. Further bone scans have shown that all the bony metastases ceased to progress since the PDT/SDT.
22	Female	51	Presented with breast cancer with several bony metastases in November 2006. We carried out PDT/SDT on her and had increased pain following the PDT/SDT. Her median survival

			time was 2 years form the date of first seeing her. At the time of writing she has stable disease.
23	Female	47	This patient came to see me in January 2007, with metastatic breast cancer, with several skin metastases and one bony metastases. Median survival time when I first saw her was one year. We carried out PDT/SDT on her in March 2007. She died in May 2008.
24	Female	51	Presented in February 2007. She had a left sided breast cancer operated on with mastectomy in January 2007. This was oestrogen receptor negative, node negative and HER2 positive. She was recommended to have chemotherapy post surgery but she turned this down. Instead she wanted to do PDT/SDT which we carried out for her in April 2007. At the time of writing she is alive and well and tumour free.

25	Female	38	Presented with metastatic breast cancer with several liver metastases and bone metastases. At the time of seeing her her median survival time was 6 months. We carried out PDT/SDT on her in May 2007. This patient died in December 2007.
26	Female	67	This patient presented with extensive recurrent breast cancer, presenting to us in August 2007 following a right sided mastectomy in 2002, followed by chemotherapy and radiotherapy in 2002. She was oestrogen receptor positive, node positive and HER2 positive. We carried out PDTSDT on her in August 2007. We covered this with Dexamethasone, 2 milligrams twice daily. She developed a big inflammatory response to tumour cell death and this gradually settled down over a period of 2-3 months and this cleared 80% of the tumour. Because there was so much tumour mass over the chest, we carried out another course of PDT/SDT in December 2007 and a significant proportion of the remaining tumour was killed off. In July 2008 she had a recurrence in the left breast and in areas of skin below the left breast. We carried out another course of PDT/SDT, again with a good response. Currently she has stable disease. On seeing her in August 2007, her median survival time was 2 years.
27	Female	57	We saw this patient in October 2007 with a right sided breast cancer, with distant metastases in the brain and the lung. Her median survival time on seeing her was 3 months. We carried out PDT/SDT on her in October. She died in January 2008.
28	Female	47	Presented November 2007 with metastatic right sided breast cancer, with several bony metastases and metastases in the right lung. On seeing her her median survival time was 3

			months. We carried out PDT/SDT on her in November 2007, under Dexamethasone cover. Initially her bone metastases produced more pain for 3 weeks post-PDT, then this improved radically. She also had a cough pre-PDT/SDT from the lung metastases in the right lung and this was significantly better a month after PDT/SDT. This patient died in March 2008.
29	Female	53	This patient initially presented in April 2005. She had had a Grade 3 tumour in the left breast, treated by lumpectomy; this was oestrogen receptor positive. At the time she turned down chemotherapy, radiotherapy and Tamoxifen. We offered her Ukraine (Chelidonium Majus & Thiotepa) in order to reduce her risk of recurrence. In February 2008 she developed a small quarter inch diameter recurrence in the scar. She refused conventional treatment and decided to do PDT/SDT. A month after PDT/SDT this tumour had halved in size. She then had it removed surgically and the pathology report showed that it contained only necrotic cells and no active tumour.
30	Female	47	This patient had a left sided breast cancer in March 2008; oestrogen receptor negative and HER2 positive. I saw her in June 2008 and she was on Herceptin at that time. She had had a mastectomy in 2008 but refused chemotherapy and radiotherapy. When I first saw her she had liver metastases. She had been offered Taxol, but was unsure as to whether to take this up. We did PDT/SDT on her in July 2008. She went on to Taxol in September 2008 and a further scan in September 2008 showed significant improvement. I last saw her mid-January 2009 and the liver secondaries had, on scan, reduced in size and she was generally feeling well, but she still had some active tumour in the left breast. At that time she was considering doing another course of PDT/SDT.
31	Female	46	Presented to me in June 2008, with a recurrence of breast cancer which had occurred 12 years previously in the right breast. At that time she had a lumpectomy and lymph-gland resection, followed by chemotherapy and radiotherapy. This time her recurrence was on the left side and started with pain in the arm. She had been offered a mastectomy, but refused this. She was also offered chemotherapy, which she agreed to. She had had breast implants put into both breasts. She refused a whole body CT and bone scan. She did one week of PDT/SDT in July 2008. This patient has been lost to follow up.
32	Female	60	Presented in June 2008 with metastatic breast cancer with metastases in the femur and both lungs. At the time of first seeing her her median survival time was 6 months. We did PDT/SDT on her in 2008. At the time of writing she is in

			reasonable health and has stable disease.
33	Female	47	This patient had left sided breast cancer; oestrogen negative and HER2 positive, diagnosed in March 2008. She had a left sided mastectomy at the end of April 2008. Chemotherapy and radiotherapy were recommended, as was Herceptin. At the end of May 2008, the scan showed spread to the liver. She refused chemotherapy and radiotherapy, but decided to have Herceptin. At the end of May 2008 she was found to have secondaries in the liver and also a recurrence in the lymph node in the left axilla. She did PDT/SDT at the end of July 2008. In December 2008, on CT scan, the liver metastases were found to be stable. She was put on Docetaxol in September 2008. She had a median survival time on first seeing her, of one year. At the moment she has stable disease and I last saw her in mid-January 2009.
34	Female	55	This patient presented in September 2008 with metastatic breast cancer with metastases in the liver, lymph nodes, bones and lung. Her median survival time at the first appointment was 3 months. We did PDT/SDT on her in September 2008, under Dexamethasone cover. At the time of writing the patient is still alive and has good quality of life.
35	Female	41	This patient had an oestrogen receptor negative, HER2 negative, right sided breast cancer when she saw me in November 2008. She had had a wide local excision. She was recommended to have chemotherapy and radiotherapy, but she turned this down. She was node negative. She wished to do PDT/SDT, which we did for her in December 2008. At the time of writing the patient is well and tumour free.
36	Female	62	Presented with recurrent breast cancer in December 2008, nineteen years after a wide local excision of her breast cancer and radiotherapy to the left breast. She presented with a 2 month history of constant pain and visual disturbance on upward gaze in the right eye. A CT revealed a secondary encasing the anterior third of the right optic nerve. She had multi-focal sclerotic lesions in the skull base and cervical spine. None of these secondaries were amenable to surgical intervention. Her median survival time at the time of seeing her was 6 months. We carried out PDT/SDT on her in December 2005 under Dexamethasone cover. Within one week of this treatment the pain in her right eye had eased to a mild ache and her visual disturbance had started to ease. She had a wheeze pre-PDT/SDT which started to improve post-PDT/SDT and her exercise ability has improved from having to stop whilst climbing a flight of stairs pre-PDT/SDT, to be able to walk for 30 mins at a time. This was 3 weeks post-follow up to PDT/SDT.

## **CERVICAL CANCER**

37	Female	51	Presented in January 2007 with recurrent carcinoma of the cervix, with a large recurrence in the pelvis and a stent in right ureter. The mass in the right side of her pelvis was causing significant swelling in the right leg. She had PDT/SDT in March 2007 and at this time her median survival time was 2 months. We carried out this treatment for one week only because of her clinical condition. Her right leg became more swollen post-PDT/SDT due to the inflammatory response of the tumour mass in the pelvis. This patient died in mid July 2007.
38	Female	51	Presented in February 2008 with recurrent CA cervix that had spread into the pelvis. At the time she had been offered chemotherapy and radiotherapy which offered a 70% chance of cure. but she refused this option. We did PDT/SDT on her in March 2008, with which she coped well. Eventually her Oncologist persuaded her to have chemotherapy and radiotherapy which she had in autumn 2008. Currently she is tumour free. It is difficult to determine whether the chemotherapy/radiotherapy or PDT/SDT, or a combination of the two, was responsible for her improvement.
39	Female	50	Presented in November 2008 with recurrent cervical cancer, with a tumour in the pelvis and para-vertebral nodes. She didn't wish to have chemotherapy. She had had previous chemotherapy with which she coped badly. We carried out PDT/SDT on her in November 2008 under Dexamethasone cover. A week after PDT/SDT she developed discomfort in the pelvic mass and the groin glands had swelled up due to the inflammatory response, as a result of tumour cell necrosis. Other than that, she has continued to improve. Her median survival time at the time of seeing her was 6 months. I last saw her in January 2009, when she was in reasonable health clinically, with a good quality of life.

## **COLORECTAL CANCER**

40	Female	64	Patient presented with metastatic colorectal cancer, with liver metastases. We treated her with PDT/SDT in August 2005, at which time her median survival time was 3 months. The patient died in October 2005.
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41	Male	56	We saw this patient in October 2005 with metastatic colorectal cancer with several liver metastases. He had been offered Irinotecan but decided not to accept this. His median survival time at the first appointment was 6 months. We carried out PDT/SDT on him in August 2005. This patient has been lost to follow up.
42	Female	66	We saw this patient in October 2005. She had had colorectal cancer diagnosed in 2003 and was treated with a hemicolectomy. On routine scanning in September 2005, she was found to have lung metastases in the left upper lobe. She had a left upper lobectomy to remove these tumours, and at that time she was recommended to have neo-adjuvant chemotherapy, but refused. She wished to do PDT/SDT which she had done in January 2006. At the time of writing this patient is alive and well and is cancer free.
43	Female	64	We saw this patient with metastatic colorectal cancer with lung and liver metastases. We carried out PDT/SDT on her in January 2006. Her median survival time at that time was 6 months. She died in July 2006.
44	Male	29	We saw this patient with metastatic colorectal cancer, with several liver metastases in October 2005, when his median survival time was 3 months. We did PDT/SDT on him in October 2005. This patient died in February 2006.
45	Male	65	We saw this patient with metastatic colorectal cancer, with several liver metastases. He is also a Type 2 diabetic and hypertensive. Median survival time when I saw him was 6 months. We carried out PDT/SDT on him in July 2006. This patient has been lost to follow up.
46	Female	48	We saw this patient with metastatic colorectal cancer, with liver metastases. We carried out PDT/SDT in January 2007, at which time her median survival time was 3 months. This patient died in March 2008.
47	Female	54	We saw this lady in October 2007. She had a squamous cell carcinoma of the anus, following a previous history of anal fissures and this was treated with radiotherapy and chemotherapy in 2006. In the first instance this patient turned down surgery and a local resection was not possible. When I saw her in October 2007 there was no local disease detectable. However, she had a liver metastasis diagnosed in April 2007. She was listed for a partial hepatectomy. She decided to do neo-adjuvant PDT/SDT before surgery, which she had in October 2007. She had a partial hepatectomy in February 2008 and on histology the metastatic lesion was found to be necrotic with no active tumour present. I saw her most recently in mid January and she is fit and well and cancer free.
48	Male	56	We saw this man with metastatic colorectal cancer with many

			peritoneal metastases. We carried out PDT/SDT on him in November 2007. He coped with this well, apart from some discomfort in the abdominal muscles post-PDT/SDT, due to an inflammatory response to tumour cell necrosis from the peritoneal secondaries. His median survival time when I saw him was 3 months. This patient died at the end of May 2008.
49	Female	48	We saw this patient with metastatic colorectal cancer with metastases in the liver and the left lung. I saw her in November 2007, at which time her median survival time was 6 months. We carried out PDT/SDT on her in April 2008. At the time of starting PDT/SDT her median survival time was 2 months. This patient died in mid October 2008.
50	Male	74	We saw this patient with carcinoma of the rectum in September 2006, for which he had refused an abdominal perineal resection. Without a perineal resection his median survival time was 12 months. We did two rounds of PDT/SDT on him, one in September 2006 and the other in August 2007. My last contact with him was in December 2008, at which time he was alive and well, but still had tumour in the rectum. Since that time he has been lost to follow up.
51	Female	70	We saw this patient with metastatic colorectal cancer, with metastases in the left lung and liver, in October 2008. She had been offered Irinotecan but turned this down. We carried out PDT/SDT on her in October 2008, at which time her median survival time was 3 months. I last saw her in January 2009, at which time she had a good quality of life, but was not tumour free.
52	Male	64	We saw this patient with colorectal cancer with a large mass in the pelvis and several lung metastases. We carried out PDT/SDT on him January 2009. The mass in the pelvis had been obstructing the right ureter; the right ureter was stented. We covered him with Dexamethasone 2 milligrams twice daily. Ten days after treatment his right leg developed a mild oedema and this gradually settled over the following week. Previous to treatment he had had significant back pain due to the pelvic mass and this began to clear up some 10 days following PDT/SDT. We are continuing to see him and he is considering another course of PDT/SDT.

### **GRANULOSA CELL TUMOUR**

53	Female	63	We saw this patient in August 2005, for her recurrent Granulosa Cell Tumour with secondaries around the portahepatis. She had been turned down for radio frequency ablation and wished to try PDT/SDT. We did this in August 2005. At that time her median survival time was one year. At the time of writing she is alive and well and relatively symptom free, but not tumour free.
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## LYMPHOMA

54	Female	60	We saw this patient with recurrent Non-Hodgkins Lymphoma, which was resistant to second-line chemotherapy. We carried out PDT/SDT on her in July 2005. At the time of writing she is in full remission and has no recurrence of tumour.
55	Male	69	We saw this patient with chemo-resistant recurrent Hodgkins Lymphoma. We did PDT/SDT on him in September 2005, when his median survival time was 3 months. He died in December 2005.
56	Female	55	We saw this patient with recurrent Non-Hodgkins Lymphoma, with a large gland on the left side of the neck. We carried out PDT/SDT on her in May 2006. Following her up in July 2006, the mass was a quarter of its original size and two other tumours in local lymph glands had disappeared. Since that time this patient has been lost to follow up.
57	Female	59	We saw this patient with chemo-resistant recurrent Non-Hodgkins Lymphoma. At the time of seeing her her median survival time was 3 months. We did PDT/SDT on her in June 2007. There was a significant reduction in tumour size a month after the PDT/SDT treatment. This patient died in January 2008.
58	Male	64	We saw this patient with chemo-resistant recurrent Non-Hodgkins Lymphoma, with extensive involvement in the abdomen. We did PDT/SDT on him in February 2008, when his median survival time was 3 months. He died at the end of July 2008.
60	Female	55	We saw this patient with recurrent Non-Hodgkins Lymphoma. We carried out PDT/SDT on her in August 2008. Post-PDT/SDT the enlarged lymph nodes had decreased in size by 40%. This patient is still alive and well and is considering further PDT/SDT.

## HEAD & NECK CANCERS

61	Male	58	We saw this patient with metastatic squamous cell carcinoma of the base of the tongue, with metastases in the right lung. His median survival time at the time I saw him was one year. We carried out PDT/SDT on him in April 2006. This patient has been lost to follow up.
62	Male	60	We saw this patient with recurrent squamous cell carcinoma

			<p>of the mouth, in October 2008. He had had surgery for his tumour, but has not had a complete clearance. He had been offered a further radical neck resection, with 25% chance of full clearance, but because of the mutilating nature of the operation he was not happy to go down the surgical route. He had also been offered chemotherapy, but had been informed that chemotherapy is generally ineffective in head and neck cancer. We carried out PDT/SDT on him in October 2008. He refused Dexamethasone to cover this procedure and a week after finishing PDT/SDT he developed significant swelling due to an inflammatory response to tumour cell necrosis in the area of the throat and cheek, for which we put him on to Dexamethasone, which at that time, he was willing to accept. However, the swelling continued and he developed problems in swallowing. He had to have a gastrostomy with an indwelling PEG tube. At the time of writing his condition is now settling and the swelling is beginning to resolve. In this case he clearly had a big response to tumour cell necrosis and the spread of the tumour was far wider than would have been covered by a radical next dissection and therefore in hindsight surgery would not have worked in clearing his residual tumour.</p>
63	Female	58	<p>I first saw this lady with squamous cell carcinoma of the larynx, following radiotherapy 20 years earlier for Hodgkins Lymphoma, in October 2006. She had been offered a laryngectomy for her squamous cell carcinoma of the larynx, with routine radiotherapy offered post-laryngectomy to reduce the risk of local recurrence. As she had had previous radiotherapy, the risks of further radiotherapy were magnified, so she decided to turn this down. Instead she did neo-adjuvant pre and post operative PDT/SDT and she got no local recurrence. However, she developed a distant recurrence under the base of the skull on the left side on November 2008 and at that time her median survival time was 2 months. We carried out PDT/SDT on her under Dexamethasone cover in November 2008. Following this she developed a trigeminal neuralgia due to scarring following an inflammatory response to tumour cell necrosis of her recurrent cancer. This was dealt with with analgesics. At the time of writing she is deteriorating and is unlikely to survive beyond the end of March 2008.</p>
64	Female	58	<p>I saw this patient with adenocarcinoma of the pallet in January 2009 with a large tumour on the left hand side of the pallet, with a large lymph gland on the right side of the neck, sufficiently large to obstruct her turning her head, with</p>

		several lymph glands on the left hand side of the neck. We carried out PDT/SDT on her in January 2009, which we did under Dexamethasone cover. A week after PDT/SDT the neck glands had reduced in size by 50% and the tumour has now become operable, with less mutilating consequences than pre-PDT/SDT. If she is to go on and have operative intervention, this would be followed by post-operative PDT/SDT.
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### **KIDNEY CANCERS**

65	Male	56	This patient was seen in February 2007, he had had kidney cancer in the left kidney 10 years ago and on seeing him in February 2007 he had secondaries in the pancreas and both lungs. His median survival time when I saw him was one year. We did PDT/SDT on him in April 2007. A scan done in August 2007 showed tumour progression. He then went on to have a monoclonal antibody. He is still alive and has a good quality of life.
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### **NON-SMALL CELL LUNG CANCER**

66	Female	80	I saw this patient in August 2005 with an inoperable non-small cell lung cancer of the left lung. She had turned down palliative radiotherapy and at the time I saw her her median survival time was 6 months. We carried out PDT/SDT on her September 2005. Following PDT/SDT she had some inter-scapula ache, but other than that she was well. We carried out a second course of PDT/SDT on her in June 2007 because up until March 2007, she had stable disease and she had tumour progression in June 2007. She did well on this course and at the time of writing she still has stable disease and is alive and well, with a good quality of life.
67	Female	37	This patient had metastatic non-small cell lung cancer with metastases in the opposite lung and also liver metastases. Her median survival time when we treated her was 3 months. We carried out PDT/SDT on her in December 2005. This patient died at the end of March 2006.
68	Female	79	We saw this patient with non-small cell lung cancer in the left upper lobe. When I saw her her median survival time was 6 months. We carried out PDT/SDT on her in June 2006. At

			the time of writing she is alive and well and has stable disease.
69	Female	61	We saw this patient with non-small cell lung cancer. We carried out PDT/SDT on her in August 2006 under Dexamethasone cover. Her median survival time was 6 months. This patient died on 24 <sup>th</sup> October 2007.
70	Male	49	We saw this patient with non-small cell lung cancer in July 2006, at which time his median survival time was 6 months. We carried out PDT/SDT on him at that time. This patient died at the end of December 2006.
71	Female	56	We saw this patient in July 2007 at which time her median survival time was 6 months. She had non-small cell lung cancer of the left lung, with a metastasis in the right adrenal gland. At the time of seeing her she had a troublesome persistent cough, which she had had for 10 months. We carried out PDT/SDT on her in July 2007 and one month after treatment her cough cleared up. Also the airflow into her left lung improved 60% one month following PDT/SDT. We did a further a course of PDT/SDT in October 2007 when she was becoming symptomatic again with breathlessness. She responded well to this until March 2008, when she developed a severe chest infection and pain in the right adrenal gland increased. She decided not to do any further PDT/SDT. At the time of writing she is alive, but has progressive disease.
72	Male	69	We saw this patient with non-small cell lung cancer in the left lung, with a secondary in the right temporal lobe. He had radiotherapy to the brain secondary, but decided not accept chemotherapy for the lung primary. We carried out PDT/SDT on him using Dexamethasone cover and at the time of treatment in November 2007, his median survival time was 3 months. He did well following PDTSDT and with no further treatment he survived until the end of December 2008.
73	Female	79	We saw this patient with non-small cell lung cancer in the right lung and metastases in the right and left gluteal muscles. When I saw her her median survival time was 3 months. We did PDT/SDT on her under Dexamethasone cover in April 2007 and her median survival time at the time of treating her was 3 months. I last saw this patient in mid July 2007 and at that time she was in reasonably good clinical condition, but still had disease. Since then she has been lost to follow up.

74	Male	67	We saw this patient with non-small cell lung cancer in the
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			right lower lobe. At the time I saw him his median survival time was 3 months. We carried out PDT/SDT on him in March 2008. A month post-PDT/SDT, his dry cough had improved, which was persistent before treatment, but he developed a left sided headache. At that time we suspected he had developed a brain secondary, which on further investigation proved to be the case. He died in May 2008.
75	Female	70	We saw this patient with non-small cell lung cancer in the left lung. She had chemotherapy in April 2008 which had been ineffective. We carried out PDT/SDT on her in November 2008. Previous to treating her she had difficulty breathing deeply and was coughing. Three weeks post-PDT/SDT she could breath more deeply and was coughing less. When I first saw her her median survival time was 4 months. At the time of writing she is alive, but still has disease.
76	Male	62	We saw this patient with non-small cell lung cancer, with metastases in the brain and in the right hip. We carried out PDT/SDT on him in October 2008, when his median survival time was 3 months. He died at the end of January 2009.
77	Female	53	We saw this patient with non-small cell lung cancer of the right lung and her median survival time at the time of seeing in March 2008 was 3 months. We carried out PDT/SDT on her and she died the beginning of August 2008.
78	Female	79	We saw this patient with non-small cell lung cancer in June 2007. She had a previous of right upper and middle lobectomy for adenocarcinoma of the lung in 1999. In January 2007 she developed a non-small cell lung cancer from the stump on the right side and she had also developed several bony metastases in the thoracic spine. When I saw her her median survival time was 6 months. We carried out PDT/SDT on her in July 2007. The pain in the bone metastases disappeared a month following PDT/SDT and she continued with stable disease until July 2008, when she developed haemoptysis. She was put on Tarceva and had four doses of radiotherapy and decided on grounds of cost not to do more PDT/SDT. She was also diagnosed in September 2008 as having a secondary in the left adrenal gland. At the time of writing she has progressive disease and is reconsidering her options re: further PDT/SDT.

## **RELAPSED ACUTE MYELOID LEUKAEMIA**

79	Female	50	I saw this patient with chemo-resistant acute myeloid leukaemia. Her Neutrophil and Lymphocyte count and platelets were persistently low. She wished to try PDT/SDT using ultrasound over both femurs, pelvis and sternum, to try and have an effect on the bone marrow. We carried this out in November 2008. On seeing her at the beginning of January 2009 we did further blood tests, but the platelets, Neutrophils, Lymphocytes remained low and we are presuming that our treatment has had no significant effect.
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## **MELANOMA**

80	Male	60	I saw this patient with metastatic melanoma in March 2006; he had been diagnosed in December 2005. He had one brain metastases. He had multiple skin metastases distributed all over the body. His median survival time when I saw him was 3 months. We carried out PDT/SDT on him in March 2006. He died in May 2006.
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## **MESOTHELIOMA**

81	Male	71	I saw this patient with a large right sided mesothelioma. At the time he had just finished chemotherapy (Alimta plus Cisplatin). The chemotherapy had been ineffective. His median survival time when I saw him was 3 months. We carried out PDT/SDT in August 2007. He died in early December 2007.
82	Male	62	I saw this patient with mesothelioma in the right lung in April 2008, when his median survival time when I saw him was 6 months. We carried out PDT/SDT on him May 2008, under Dexamethasone cover. At the time of writing he was still alive, but has tumour progression with increased breathlessness and he has decided not to carry out any further treatment.
83	Male	67	I saw this patient with mesothelioma in the right lung, in July 2008, when his median survival time was 6 months. He refused radiotherapy and chemotherapy and wished to try PDT/SDT. At the time of writing he is still alive and has had one dose of Alimta chemotherapy agent, at the recommendation of his Oncologist. He reacted badly to this

		and his condition deteriorated soon after the chemotherapy. At the time of writing he is in a hospice and is unlikely to survive beyond the end of February.
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### **NEURO-ENDOCRINE TUMOURS**

84	Female	39	This patient had had a bronchial carcinoid removed from the right lung by lobectomy in 2000. She became pregnant in 2003 and at that time she was found to have several liver metastases from her previous carcinoid. She was put on Sandostatin injections, but this did not work. She had MIBG in November 2003, but she felt this made her worse and she developed radiation sickness. When I saw her in June 2005, she had been offered an experimental radioactively labelled drug which on the basis of her previous experience with MIBG, she decided not to take up. We carried out PDT/SDT on her in December 2005 and after the treatment course she felt significantly better. Her median survival time at the time I first saw her was 6 months. She died in April 2006.
85	Female	50	This patient had an extensive neuro-endocrine tumour, with many bone metastases in all the major bones. Because of the extensive nature of the disease and because of her clinical state, we decided to limit PDT/SDT to one week of treatment, which we carried out in November 2006. Following this one week she developed increased pain in all her bone secondaries, which was managed with Dexamethasone. We decided not to do another week of treatment. She has continued on conventional treatment. Her median survival time when I saw her in 2006 was one year. She is still alive with progressive disease at the time of writing.

## OESOPHAGEAL CANCER

86	Male	56	This patient with carcinoma of the oesophagus presented in April 2006. We carried out PDT/SDT on him in April 2006 under Dexamethasone cover. His median survival time at that time was 3 months. He died in June 2006.
87	Male	47	I saw this patient in April 2006 with oesophageal cancer which was originally diagnosed in December 2004. He had had chemotherapy followed by surgery, but reacted very badly to the chemotherapy. In November 2005 he had lower back problems and a CT scan showed bony metastases. In January 2006 he had T11 vertebrae replaced, but post surgery got numbness in the right hand and the right leg. When I saw him he had several brain lesions and was on Dexamethasone and had had whole brain radiotherapy. His median survival time when I saw him was 2 months. We carried out PDT/SDT on him under Dexamethasone cover in May 2006. He died in July 2006.
88	Male	64	I saw this patient in September 2007 with oesophageal cancer. He had refused all conventional treatment approaches and wanted to do PDT/SDT, which we did on him, under Dexamethasone cover in November 2007. He had a stent in place when I first saw him. His median survival time at that time was 3 months. I saw him again in December 2007, at which time he was significantly better. His appetite was improved and his swallowing was significantly easier. At the time of writing the patient has been lost to further follow up.
89	Male	61	This patient came to see me December 2007 with inoperable carcinoma of oesophagus with liver metastases. He was only able to swallow fluids when I first saw him. In his previous history 20 years ago he had a hiatus hernia and had reflux oesophagitis for many years. We did PDT/SDT on him under Dexamethasone cover in January 2008. At that time his median survival time was 2 months. This patient died in April 2008.

## OVARIAN CANCER

90	Female	62	We saw this patient with stage 1C ovarian cancer in March 2005. She refused all conventional treatment approaches. Her median survival time was unknown when I first saw her, but the chances of a recurrence even with effective treatment, were high. We carried out PDT/SDT on her in July 2005. At the time of writing she is still tumour free and has not had any further treatment approaches ie: no chemotherapy.
91	Female	62	This patient presented with recurrent ovarian cancer in August 2005, with a median survival time of 3 months. We carried out PDT/SDT on her in August 2005. She died in June 2006.
92	Female	50	This patient with recurrent carcinoma of the ovary, presented in November 2005. Her median survival time when I saw her was 3 months. We carried out PDT/SDT on her in December 2005. This patient died in March 2006.
93	Female	52	This patient presented in February 2006 with a recurrent ovarian cancer. She refused chemotherapy and wanted to try PDT/SDT, which she did in February 2006. Her median survival at that time was 6 months. This patient has been lost to follow up.
94	Female	63	This patient presented with a recurrent ovarian cancer in October 2006. She had a large pelvic recurrence. We did PDT/SDT on her in October 2006. A week after PDT/SDT she lost a large piece of necrotic tumour through her vagina. She developed some discomfort in her abdomen post-PDT/SDT which we controlled using Dexamethasone. When I saw her her median survival time was 3 months. A scan 3 months following PDT/SDT showed a reduction in pelvic mass. This patient died at the beginning of March 2007.
95	Female	43	This patient had recurrent ovarian cancer. We carried out PDT/SDT on her in May 2007. At that time her median survival time was 3 months. She died at the end of October 2007.

## PANCREATIC CANCER

96	Male	70	This patient presented in April 2006 with recurrent carcinoma of the pancreas, with secondaries in the lungs and throat.
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			When I saw him his median survival time was 2 months. We did PDT/SDT on him under Dexamethasone cover in May 2006. He tolerated this well. He died at the end of July 2006.
97	Male	61	This patient presented with pancreatic cancer both in the head and the tail of the pancreas, in September 2007. His median survival time at the time of seeing was 2 months. We carried out PDT/SDT on him in December 2007. He died at the end of February 2008.
98	Female	77	This patient was found to have a carcinoma of the pancreas on routine body scan. She also had longstanding myelodysplasia. Surgery was suggested, but she turned this down. She wanted to try PDT/SDT, but she refused to have this covered with Dexamethasone. We carried out PDT/SDT on her in December 2007. One week after completion of PDT/SDT she collapsed with a left sided hemiparesis. A CT scan showed a cerebral infarct and it was concluded that the myelodysplasia made her more likely to develop a left hemiparesis. This patient's median survival time was 6 months when I saw her. However, she died as a result of the hemiparesis at the end of December 2007.

### **PERITONEAL CANCER**

99	Male	57	This patient presented with chemo-resistant peritoneal cancer in January 2006. At the time of seeing him his median survival time was 3 months. We carried out PDT/SDT on him in January 2006. He died at the end of February 2006.
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### **PROSTATE CANCER**

100	Male	72	I first saw this patient in June 2005 with hormone resistant prostate cancer, with multiple bony metastases in the pelvis. At the time of seeing him his median survival time was 4 months. We did PDT/SDT on him in June 2005 and the pain in the bony metastases was initially aggravated, but then resolved 2 months later. This patient died early December
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			2005.
101	Male	71	I saw this patient with a recurrent prostate cancer in September 2005. He had a prostate cancer diagnosed in January 2004 following a trans-urethral resection. He had a prostatectomy in February 2004 and one lymph node was involved. When he came to see me his PSA was doubling every 3 months. Casodex was recommended, which he went on to. His median survival time was unclear when I first saw him. We carried out PDT/SDT on him in October 2005. He continued to do well until September 2006 when his PSA went up again. We recommended further PDT/SDT, but he was unable to make a decision on this at the time. He died from a stroke in September 2008.
102	Male	59	I saw this patient in January 2006. He had had a prostatectomy for a Gleason 7 prostate cancer in December 2005. When I saw him his PSA was less than 0.2. He was recommended radiotherapy post-surgery, but he decided to turn this down. In his family history his father had died of prostate cancer. We carried out PDT/SDT on him in January 2006. I saw him again in November 2006 and his PSA was still undetectable at that time. His PSA started to rise again in 2008 and he is having some local radiotherapy to deal with that.
103	Male	55	I saw this patient in July 2006 with metastatic prostate cancer. He had several bony secondaries. We carried out PDT/SDT on him in August 2006. The pain in his bony secondaries increased some 3 weeks post-PDT/SDT, then it settled. Median survival time at the time of his first appointment was 6 months. This patient died in July 2008.
104	Male	66	I saw this patient in September 2006 with a recurrent prostate cancer and also recurrent pancreatic cancer. We carried out PDT/SDT on him in November 2006. His median survival time when I saw him was 6 months. This patient died in August 2008.
105	Male	59	I first saw this patient in December 2008 with metastatic prostate cancer, with multiple bony metastases. His median survival time when I first saw him was one year. We did PDT/SDT on him in December 2006. Post PDT/SDT his PSA went up, which can happen in some cases as PSA is an intra-cellular protein, so therefore on tumour cell necrosis, due to the PDT/SDT, this can initially raise PSA levels. His PSA continued to remain up for 9 months. The pain in his bony metastases improved 2 months following the PDT/SDT. Currently he is alive, but has several more bony metastases, but remains pain free.
106	Male	66	This patient came to see me in July 2006. He had prostate cancer in the left side of the prostate, with some extra

			capsular extension and some lymph gland involvement. We carried out 2 rounds of PDT/SDT on him in August and December 2006. Currently he is well and his tumour is stable. There is no metastatic spread. His median survival was not possible to calculate when I first saw him.
107	Male	57	This patient had prostate cancer with lymphatic spread and liver metastases, but no bone metastases. His median survival time when I saw him was 2 months. We carried out one weeks course of PDT/SDT on him in January 2008; he was not well enough to consider doing a two week course. This patient died in March 2008.

## **SARCOMAS**

108	Female	42	This patient came to see me in September 2005. She was diagnosed with a leiomyosarcoma in December 2004. When she presented to me she had secondaries near to the heart, pancreas and several metastases in the lungs. At the first appointment she had a median survival time of 3 months. We did PDT/SDT on her in November 2005. This patient died at the end of March 2006.
109	Female	50	This patient came to see me in September 2008. She had had a synovial sarcoma in the left leg, which was dealt with operatively and when she saw me she had lung metastases and metastases in the pericardium. We did PDT/SDT on her in November 2008. Her median survival time when I saw her was 6 months. We did this under Dexamethasone cover. At the time of writing she is fit and well and no further scans have been done on her.
110	Female	34	This patient had a fibrosarcoma in the upper left chest, causing difficulty with abduction of the left shoulder. She had an excision of this tumour in 2004, but it had recurred. She had been offered a wide local excision followed by radiotherapy, but she did not wish to follow this treatment option. We carried out PDT/SDT on her in April 2006. This patient has been lost to follow-up.

## **SMALL CELL LUNG CANCER**

111	Female	61	This patient had a small cell lung cancer. She had
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			chemotherapy and we also carried out PDT/SDT on her in August 2005. Interestingly in this patient, 2-3 weeks after PDT she noticed her hair started to regrow and previous to that her hair had been falling out. Subsequent scans showed an 80% reduction in tumour size. This patient's median survival time when I first saw her was one year. This patient is still alive and well and tumour free.
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### **STOMACH CANCER**

112	Female	45	This patient presented with recurrent stomach cancer. She had a median survival time of 3 months when I saw her. We carried out PDT/SDT on her in September 2005. She died in November 2005.
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### **URACHAL TUMOURS**

113	Female	39	Female age 39. This patient presented with a recurrent urachal tumour in November 2006. At the time I saw her she had a median survival time of 6 months. We carried out PDT/SDT in November 2006. This patient died in May 2008.
114	Male	63	This patient saw me in March 2008 with a recurrent urachal tumour which had been originally diagnosed in September 2007. He had a significant amount of tumour mass in his abdomen and his median survival time was 3 months when I saw him. We carried out PDT/SDT on him in March 2008, under Dexamethasone cover. The tumour mass in the abdomen diminished significantly 2 months post-PDT/SDT. He had a nephrostomy and he was passing blood-stained urine through this, but this cleared up 3 months after the PDT/SDT. He also began to put weight back on following the PDT/SDT. This patient died in December 2008.

### **CARCINOMA OF UNKNOWN PRIMARY**

115	Female	40	I saw this patient in January 2008 with carcinoma of unknown primary, presenting as a pelvic mass. She had had debulking surgery in May 2007. median survival time was impossible to predict. We did PDT/SDT on her in January 2008 and she coped well with this. A scan at the end of May 2008 showed the tumour reduced in size and
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			had taken on a nodular appearance. She had another scan in September 2008 which then showed tumour progression. She decided not to do further PDT/SDT.
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## **Scientific information regarding Next Generation Photodynamic Therapy:**

Although currently not available at The Dove Clinic, it is possible to use a fluorescent camera in order to image the patient's tumour, if it is relatively near the skin.

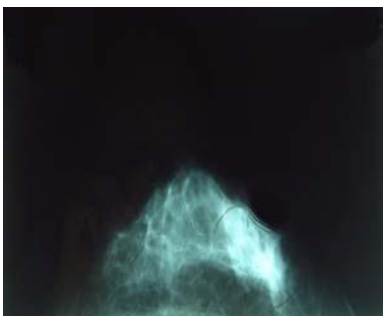
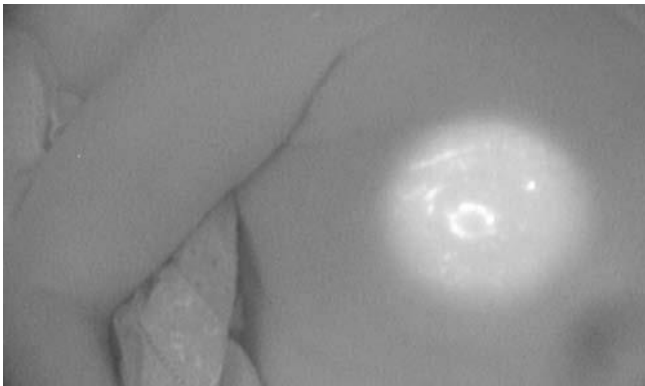
### Observational outcomes from Australian clinic using similar methods

The following is a brief summary of results obtained with recent consecutive patients who have been treated with a combination of photodynamic therapy and Sonodynamic therapy (abbreviated in this document as SPDT). These patients are from a clinic in Australia who are using the same approach as ourselves.

1. Stage III breast cancer. Primary breast tumour plus metastases in the axillary lymph node, the other breast and the liver. After SPDT and lumpectomy: no evidence of cancer in all four sites
2. Stage IV breast cancer with rampant bony metastases. Very low energy, not enough to work in the garden. In bed by 7.30 pm. After SPDT (ongoing) weight increased 3 kg and now normal. Normal sleeping time and energy levels. Resumed gardening. Scan shows that the tumours have stopped spreading.
3. Metastatic melanoma grade IV. About 80 metastases visible. Oncologist predicted 2 more months of life. After SPDT (ongoing), Alive and well 4 months after above prediction. Metastases down to about 20. Energy, appetite and weight improved. Physician estimates that about 80 % of the cancer is gone. Further treatment needed.
4. Prostate cancer (large tumour mass), grade IV, urinary infections, bowel infections. Inability to urinate without catheter, impotent. After SPDT/SDT (ongoing) prostate shrinking and softening, urination better, impotence easing. Needs further treatment but improving.
5. Ovarian cancer grade IV. Had hysterectomy and other surgery. No symptoms other than elevated cancer marker. After SPDT cancer marker now normal. No evidence of cancer
6. Squamous cell carcinoma grade I. Lump on upper lip removed surgically. PDD showed 6 metastases on upper lip. After SPDT all metastases have disappeared

7. Prostate grade IV. Hard prostate with 2 nodules, metastasized outside the gland. After SPDT (ongoing) Prostate shrunk, softened, one nodule disappeared. Better urination. Clear or almost clear of cancer.
8. Mesothelioma and lung cancer. Symptoms include coughing at night, disturbed sleep. Painful breathing, not allowing deep inhalations. Photodynamic diagnosis showed over 12 metastases on the thorax. No noticeable benefits from chemotherapy. After SPDT/SDT (ongoing). Coughing at night has stopped, giving much better sleep. Breathing not as painful, allowing deeper inhalation. "I have an amazing increase in energy ". Visible metastases have dropped from 12 or more to one.
9. Breast cancer grade IV. Lumpectomy. PDD showed metastases in the breast and the axillary lymph nodes. After SPDT (ongoing) Cleared metastases from the breast. Those in the lymph glands remain. Next treatment will be SPDT/SDT
10. Breast cancer grade IV with extensive liver metastases. SPDT failed to halt the progress of the illness. SDT was not available at the time and she has chosen other treatment.

## Breast Cancer





A non-toxic treatment for primary and metastatic cancer and other diseases



Next Generation Photodynamic Therapy as well as being used for cancer is also increasingly commonly being used for cardiovascular diseases, generalised hardening of the arteries and calcification of the arteries, as well as for Rheumatoid Arthritis. Recently studies have been carried out on HIV and AIDS, which would imply that it, may be of use in severe Chronic Fatigue Syndrome and also in ophthalmology, particularly macular degeneration. There are many papers on the use of PDT in ophthalmology.

Some scientific papers from several thousand papers in the scientific literature on PDT

## **Photodynamic therapy for lung cancer: state of the art and expanded indications**

*T Okunaka and H Kato*

*Department of Surgery, Tokyo Medical University, Tokyo, Japan.*

Nippon Geka Gakkai Zasshi, February 1, 2002; 103(2): 258-62

Commentary: Photodynamic therapy (PDT) has now achieved the status of a standard treatment modality for centrally located, early-stage lung cancer and is introduced on the home page of the US National Cancer Institute. As increasing number of patients consider quality of life after therapy, the indications for PDT are expected to expand. The success in clinical trials of PDT for cancer treatment offers encouragement for its future use.

## **Generation of effective antitumor vaccines using photodynamic therapy.**

*SO Gollnick, L Vaughan, and BW Henderson*

*PDT Center, Roswell Park Cancer Institute, Buffalo, New York 14263, USA.  
[Sandra.Gollnick@roswellpark.org](mailto:Sandra.Gollnick@roswellpark.org)*

**Cancer Res.**, March 15, 2002; 62(6): 1604-8.

*Commentary:* Preclinical studies have shown that photodynamic therapy (PDT) of tumors augments the host antitumor immune response. We found that the PDT-generated tumor cell lysates were potent vaccines and that PDT-generated vaccines are more effective than other modes of creating whole tumor vaccines, i.e., UV or ionizing irradiation, and unlike other traditional vaccines, PDT vaccines do not require coadministration of an adjuvant to be effective. PDT vaccines are tumor specific and appear to induce a cytotoxic T-cell response. Our results show that PDT effects on tumor cells alone are sufficient to generate an antitumor immune response, indicating that the direct tumor effects of PDT play an important role in enhancing that host antitumor immune response.

## Photodynamic therapy of loco regional breast cancer recurrences using a chlorin-type photosensitizer.

*P Wyss, V Schwarz, D Dobler-Girdziunaite, R Hornung, H Walt, A Degen, and M Fehr*

*Department of Obstetrics and Gynecology, University Hospital, Zürich, Switzerland. [Pius.Wyss@fhk.usz.ch](mailto:Pius.Wyss@fhk.usz.ch)*

Int J **Cancer**, September 1, 2001; 93(5): 720-4

*Commentary:* Chest wall recurrences are a frequent problem in patients treated by mastectomy for breast cancer. Surgery and ionizing radiation are established treatment modalities in these cases. Photodynamic therapy (PDT) provides an alternative treatment modality using a photosensitizer and laser light to induce selective tumor necrosis. PDT using m-THPC resulted in complete response in all patients. Response to treatment did not differ when using the 2 different drug dose protocols. Healing time depended mainly on the size of the illumination field but not on the light dose. Pain score usually rose 1 day after PDT and lasted at higher levels for about 10 days. Healing time usually ranged between 8--10 weeks. Photodynamic technique offers a minimal-invasive, outpatient treatment modality for recurrent breast cancer on the chest wall with few side effects, high patient's satisfaction and with possible repetitive application.

## **Photodynamic therapy for nonmelanoma skin **cancers**. Current review and update.**

*NC Zeitouni, AR Oseroff, and S Shieh*

*Department of Dermatology, Roswell Park **Cancer** Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. [nathalie.zeitouni@roswellpark.org](mailto:nathalie.zeitouni@roswellpark.org)*

Mol Immunol, July 1, 2003; 39(17-18): 1133-6.

*Commentary:* Photodynamic therapy (PDT) is a therapeutic modality involving the use of a photosensitizing agent activated by light to destroy tumor cells. Over the past 25 years, PDT has been shown useful in the treatment of actinic keratoses and certain nonmelanoma skin **cancers**, such as Bowen's disease and basal cell carcinoma. . PDT offers many advantages including its non-invasiveness and its ability to treat multiple lesions simultaneously and is, therefore, an interesting alternative for treating certain skin malignancies.

## **[Photodynamic therapy of dysplasias and early carcinomas in Barrett esophagus with a diode laser system--a pilot study]**

*T Zopf, A Rosenbaum, D Apel, R Jakobs, JC Arnold, and JF Riemann*

*Medizinische Klinik C, Klinikum der Stadt Ludwigshafen gGmbH.  
[thomas.zoepf@t-online.de](mailto:thomas.zoepf@t-online.de)*

Med Klin (Munich), April 15, 2001; 96(4): 212-6.

*Commentary:* Photodynamic therapy (PDT) of dysplasia and early cancer of the esophagus could show good results in the potential of ablation. Unfortunately, the existing expensive and temperamental dye laser systems foiled a broad clinical use. In this pilot study, we investigated the feasibility of an inexpensive and maintenance-free diode laser system for PDT of dysplasia and early cancer in Barrett's esophagus. PATIENTS AND METHODS: Eight patients with Barrett's esophagus and/or early cancer were treated. As light source we used a diode laser system with a maximum power output of 2 W and a wavelength of 633 +/- 3 nm. One patient was treated initially with Photosan-3, seven patients received 5-aminolevulinic acid. RESULTS: In all patients we could achieve reduction in length and/or histologically proven downgrading. In three quarters of the patients, complete eradication of adenocarcinoma could be attained. Columnar-lined metaplastic epithelium could also be completely eradicated. CONCLUSION: PDT using a diode laser system is comparably effective in Barrett's esophagus/early cancer as PDT with dye laser systems. PDT is a gentle and effective technique with little side effects.

## **An update on photodynamic therapy applications.**

*TJ Dougherty*

*Photodynamic Therapy Center, Roswell Park **Cancer** Institute, Buffalo, New York  
14263, USA.*

J Clin Laser Med Surg, February 1, 2002; 20(1): 3-7.

*Commentary:* Photodynamic therapy (PDT), following health agency approvals throughout the world for various **cancers** and other diseases, is slowly being accepted as a standard treatment to be added to the medical practitioner's armamentarium. Mechanistically, the recognition of apoptosis as an important mode of cell death following PDT and the critical role of the inflammatory process and immunity has only recently been recognized.

## **Photodynamic therapy for palliation of nonresectable bile duct cancer--preliminary results with a new diode laser system.**

*T Zoepf, R Jakobs, JC Arnold, D Apel, A Rosenbaum, and JF Riemann*

*Department of Gastroenterology, Academic Teaching Hospital, Ludwigshafen, Germany.*

Am J Gastroenterol, July 1, 2001; 96(7): 2093-7.

Preliminary results of photodynamic therapy (PDT) of bile duct cancer have shown astonishingly good results in the reduction of cholestasis, improvement of quality of life, and even prolongation of the survival time. RESULTS: Four weeks after initial PDT all patients showed a marked reduction of bile duct stenosis. CONCLUSION: PDT with the diode laser system seems to be effective in reducing malignant bile duct stenosis. This treatment is minimally invasive and has a low specific complication rate.

Pancreas, October 1, 2003; 27(3): E42-E45.

## **Infrared Laser Activation of Indocyanine Green Inhibits Growth in Human Pancreatic Cancer.**

*William W. Tseng, Romaine E. Saxton, Adriana Deganutti, and Carson D. Liu*

*Northwestern University, Feinberg School of Medicine, Chicago, Illinois; dagger Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, California; and double dagger Department of Surgery, Century City Hospital, Los Angeles, California.*

Indocyanine green (ICG) is a clinically approved, water-soluble dye that generates reactive singlet oxygen when activated by infrared light. Infrared light offers the advantage of deeper tissue penetration making ICG photodynamic therapy (PDT) ideal for treatment of intra-abdominal cancers such as pancreatic adenocarcinoma. AIMS CONCLUSION ICG PDT induces consistent and dramatic pancreatic cancer cell death. Since neither ICG nor laser alone caused toxicity, combination therapy may offer effective control of tumor growth with minimal side effects in patients with unresectable primary or metastatic pancreatic cancer.

**Phase II clinical study of photodynamic therapy using mono-L-aspartyl chlorin e6 and diode laser for early superficial squamous cell carcinoma of the lung.**

*H Kato, K Furukawa, M Sato, T Okunaka, Y Kusunoki, M Kawahara, M Fukuoka, T Miyazawa, T Yana, K Matsui, T Shiraishi, and H Horinouchi*

*Department of Surgery, Tokyo Medical University, 6-7-1 Nishi-shinjuku, Shinjuku-ku, Tokyo 160-0023, Japan.*

Lung **Cancer**, October 1, 2003; 42(1): 103-11

Photofrin is the most commonly used photosensitizer for photodynamic therapy (PDT). The major side effect of Photofrin is cutaneous photosensitivity. A second generation photosensitizer, mono-L-aspartyl chlorin e6 (NPe6) has shown anti-tumor efficacy and rapid clearance from skin. The histologic type of the tumor had to squamous cell carcinoma. No serious adverse drug reactions were observed. Complete response (CR) was seen in 84.6% of lesions (82.9% of patients). This study demonstrated excellent anti-tumor effects and safety, especially low skin photosensitivity in patients with early stage lung cancer. PDT using the second generation photosensitizer NPe6 and a diode laser will likely become a standard modality of PDT for central type early superficial squamous cell carcinoma of the lung.

## The immunological consequences of photodynamic treatment of cancer, a literature review.

*FH van Duijnhoven, RI Aalbers, JP Rovers, OT Terpstra, and PJ Kuppen*

*Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands.*

Immunobiology, January 1, 2003; 207(2): 105-13.

In this review we discuss the effect of photodynamic treatment (PDT) of solid tumors on the immune response. We have summarized the evidence that PDT causes or enhances an anti-tumor response. PDT is a local treatment in which the treated tumor remains in situ while the immune system is only locally affected and still functional in contrast with e.g. after systemic chemotherapy. We conclude that PDT of cancer is a way of in situ vaccination to induce a systemic antitumour response. In general, immune cells are found in the tumor stroma, separated from tumor cells by extra cellular matrix and basal membrane-like structures. We hypothesize that PDT destroys the structure of a tumor, thereby enabling direct interaction between immune cells and tumor cells resulting in the systemic anti-tumor immune response.

## **The role of apoptosis in response to photodynamic therapy: what, where, why, and how.**

*NL Oleinick, RL Morris, and I Belichenko*

*Department of Radiation Oncology and the CWRU/UHC Ireland Comprehensive  
**Cancer** Center, School of Medicine, Case Western Reserve University,  
Cleveland, Ohio, USA. [nlo@po.cwru.edu](mailto:nlo@po.cwru.edu)*

Photochem Photobiol Sci, January 1, 2002; 1(1): 1-21.

Photodynamic therapy (PDT), a treatment for cancer and for certain benign conditions, utilizes a photosensitizer and light to produce reactive oxygen in cells. PDT is primarily employed to kill tumor and other abnormal cells, so it is important to ask how this occurs. Many of the photosensitizers currently in clinical or pre-clinical studies of PDT localize in or have a major influence on mitochondria, and PDT is a strong inducer of apoptosis in many situations

## **Preliminary report of photodynamic therapy for intraperitoneal sarcomatosis.**

*TW Bauer, SM Hahn, FR Spitz, A Kachur, E Glatstein, and DL Fraker*

*Department of Surgery, School of Medicine, University of Pennsylvania,  
Philadelphia 19104, USA.*

Ann. Surg. Oncol., April 1, 2001; 8(3): 254-9.

Sarcomatosis is the disseminated intraperitoneal spread of sarcoma. It is a condition for which there is no effective treatment. Photodynamic therapy (PDT) is a cancer treatment modality that uses a photosensitizing agent and laser light to kill cells. Five patients (45%) have no evidence of disease at follow-up (range, 1.7-17.3 months), including patients at 13.8 and 17.3 months examined by CT. Two patients (18%) died from disease progression. Four patients (36%) are alive with disease progression.

**CONCLUSIONS:** Debulking surgery with intraperitoneal PDT for sarcomatosis is feasible. Preliminary response data suggest prolonged relapse-free survival in some patients.

**Effective treatment of liver metastases with photodynamic therapy, using the second-generation photosensitizer meta-tetra(hydroxyphenyl)chlorin (mTHPC), in a rat model.**

*JP Rovers, AE Saarnak, A Molina, JJ Schuitmaker, HJ Sterenberg, and OT Terpstra*

*Department of Surgery, Leiden University Medical Centre, The Netherlands*

Br J **Cancer**, October 1, 1999; 81(4): 600-8.

The only curative treatment for patients with liver metastases to date is surgery, but few patients are suitable candidates for hepatic resection. The majority of patients will have to rely on other treatment modalities for palliation. Photodynamic therapy (PDT) could be a selective, minimally invasive treatment for patients with liver metastases. . Damage to normal liver tissue was mild and transient as serum aspartate aminotransferase and alanine aminotransferase levels normalized within a week after PDT treatment. Long-term effects of mTHPC-PDT were studied on day 28 after treatment. Regardless of drug dose and drug-light interval, PDT with mTHPC resulted in complete tumour remission in 27 out of 31 treated animals (87%), with only four animals in which tumour regrowth was observed. Non-responding tumours proved to be significantly larger ( $P < 0.001$ ) in size before PDT treatment. This study demonstrates that mTHPC is retained in an intrahepatic tumour and that mTHPC-PDT is capable of inducing complete tumour remission of liver tumours.

## **Photodynamic therapy: a novel treatment for primary brain malignancy.**

*TT Goodell and PJ Muller*

*Oregon Medical Laser Center/Providence St. Vincent Medical Center, 9205 SW Barnes Road, Portland, OR 97225, USA.*

J Neurosci Nurs, December 1, 2001; 33(6): 296-300

Providing therapy that conserves healthy brain tissue while effectively killing cancerous tissue remains a major challenge in the treatment of primary malignant brain tumors. The most common primary brain malignancies tend to recur despite intensive therapy, and the side effects of radiotherapy and chemotherapy can have considerable influence on health and quality of life. Photodynamic therapy (PDT) is a new technology being investigated to fulfill the need for a targeted cancer treatment that may reduce tumor recurrence and extend survival with few adverse effects. An investigational treatment, PDT employs wavelength-specific light in combination with a photosensitizing agent. The photosensitizing agent accumulates in tumor cells and is activated by nonthermal light, producing radical oxygen species that locally kill tumor cells. The selectivity of the process makes PDT appealing in the brain, where conservation of healthy tissue is vital. Many new photosensitizing compounds and varying methods of light delivery are being studied. This technology shows promise for the treatment of primary brain malignancies.

## **Scientific References in the Use of Photodynamic Therapy in Cardiovascular Diseases**

### Motexafin Lutetium (Cardiovascular Diseases) Phase II Trial

A Phase II, Double blind, Multicenter, Randomized Clinical Trial of Motexafin Lutetium Injection and Far-Red Light Activation for the Prevention of Restenosis and Primary Treatment of De Novo Atherosclerotic Lesions in Femoral and Popliteal Arteries

Principal Investigator: Paul Kramer, MD, Kramer and Crouse Cardiology, Mid America Heart Institute, Kansas City Missouri

Institutional ID Number: PCYC-0502 (Closed)

### Motexafin Lutetium (Cardiovascular Diseases) Phase I Trial

A Phase I, Drug and Light Dose-Escalation Clinical Trial of Antrin® (Motexafin Lutetium) Injection and Far-Red Light Activation (Phototherapy) in Subjects with Coronary Artery Disease Undergoing Percutaneous Coronary Intervention (PCI) with Stent Placement

Principal Investigator: Dean Kereiakes, MD, Lindner Research Center, Christ Hospital, Cincinnati, OH

Institutional ID Number PCYC-0551 (Completed)

Kereiakes, et al; Circulation 108: 1310-1315, 2003

Photodynamic Therapy for Prostate Cancer — A Novel Technique for Assessing Light Transmission in the Prostate

*CM Moore, CA Mosse, I Hoh, H Payne, D Rickards, SG Bown, ME Emberton  
United Kingdom, National Medical Laser Centre, University College London,  
London, UK, Myerstein Institute of Oncology, University College London  
Hospitals Trust, London, UK, Department of Imaging, University College London  
Hospitals Trust, London, UK, Institute of Urology, University College London,  
London.*

#### Aims:

Photodynamic therapy (PDT) uses a light activated drug to cause necrosis, whose depth depends on the penetration depth (PD) of light. Previous studies have measured PD in up to three positions per prostate with wavelengths of up to 665nm. These wavelengths can be absorbed by haemoglobin, leading to large variation in PD. Newer drugs are activated by light of longer wavelengths. It is predicted that they will have increased PD and will not be absorbed by haemoglobin. We aimed to use a novel technique to determine PD in multiple positions throughout the prostate, with 763 nm light.

#### Procedures

Patients having high dose rate (HDR) brachytherapy for prostate cancer have multiple transparent plastic needles in the prostate for two days. These are used to carry radioactive iridium wires but are also suitable for carrying optical fibres. Laser light was delivered along the needles using a cylindrically diffusing optical fibre. An isotropic detector was placed sequentially in nearby needles and optical power at different distances from the source was measured with a light meter. Needle separation was measured on CT.

#### Major Findings

PD is the depth at which 63% of light intensity is lost. It is calculated from the diffusion theory approximation to the Boltzmann transport equation. The mean PD over 600 readings was 5.5 mm (2.7-12.1mm).

#### Significance

The PD showed greater variability than expected. As this variation is proportional to the depth aimed to treat, absolute variation will need to be minimised by reducing the needle separation to less than 10 mm.

## Conclusion

PDT for prostate cancer will require multiple interstitial light sources, similar to the needle configuration used for HDR brachytherapy.

## Photodynamic Therapy for Primary Prostate Cancer — A Pilot Study using MTHPC

*CM Moore, TR Nathan, WR Lees, A Freeman, CA Mosse, M Emberton, SG Bown*

United Kingdom, National Medical Laser Centre, University College London, London, UK, Department of Imaging, University College London Hospitals Trust, London, UK, Department of Histology, University College London Hospitals Trust, London, UK, Institute of Urology, University College London, London

### Aims:

To determine whether photodynamic therapy (PDT) using meso tatra hydroxy phenyl chlorin (mTHPC) could be a primary treatment for organ confined prostate cancer.

### Procedure

Six men with histologically proven prostate cancer, who were unsuitable for or declined radiotherapy, surgery or active surveillance, were studied. The mean pre-treatment PSA was 7.7 ng/ml (range 2.7-15), with a Gleason score of 3+3 in all patients.

The photosensitiser mTHPC was given intravenously and activated after 2-5 days by 652 nm light delivered transperineally to the prostate using MRI guidance. Areas of cancer were treated under local anaesthetic and sedation according to MRI or biopsy results. The peripheral zone of the same lobe was also treated. 4 out of 6 patients had 2 treatments.

### Major Findings

Early MRI changes indicated extensive oedema, with patches of ill defined necrosis. This necrosis was well defined at 1 month and was not seen at 3 months. Histology revealed areas of necrosis and fibrosis at 1 month and fibrosis at 2 months. 8 out 10 treatments resulted in a PSA reduction (mean reduction per patient 4.0 ng/ml, range 2.0 — 10).

2 treatments led to catheterisation for 9 to 19 days respectively. 1 patient had incontinence requiring 1 pad per day for 4 months following a 2<sup>nd</sup> PDT treatment.

## Significance

This is the first report of the use of PDT as a primary treatment for prostate cancer. Necrosis followed by fibrosis, and a PSA reduction was seen.

## Conclusion

PDT for primary prostate cancer merits further investigation.

JOURNAL OF UROLOGY 2002 October 168:1427-32.

Fourteen patients with rising PSA levels and with a proven local recurrence after treatment with the radiation were given PDT. PSA scores decreased in 9 patients, to undetectable levels in two of them. Five patients had no viable tumour when a needle biopsy was taken after treatment and CT and MRI scans showed clear signs of tumour necrosis involving up to 91% of the prostate after treatment with PDT. The authors of this study concluded the photodynamic therapy can destroy localized areas of cancer with safe healing without cumulative toxicity associated with ionizing radiation. This study, and the previous two studies, used fibre-optic cables inserted into the prostate. This itself caused some side effects in that 4 men developed stress-incontinence in the Journal of Urology Study and 4 suffered long term impotence. With the use of Next Generation PDT, because it's so tumour specific, the insertion of fibre-optics into the prostate is not necessary.

Please also see the paper by Duijnhoven et al from Immunobiology January 1<sup>st</sup> 2003, relating to this issue.