

Particle beams for cancer therapy

A look at the emergence of alternatives to radiotherapy which still has serious side-effects and damages tissue unaffected by cancer.

Despite technical improvements in X-ray based radiotherapy delivery, there should be no complacency regarding side-effects that occur during and after treatment: these can be both serious and persistent. High energy X-rays pass through the entire thickness of the body wherever they are used, with unnecessary exposure of many organs. Recently, progress has been achieved using charged particles such as protons and carbon ions. These particles deposit energy far more selectively than X-rays due to the 'Bragg-peak' effect (Figure 1).

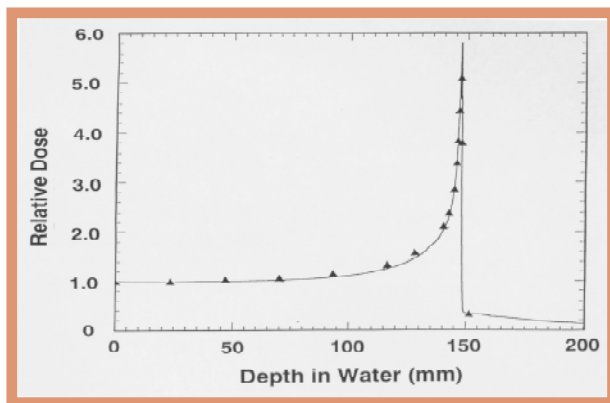


Figure 1: Example of a Bragg peak measured in water at the national Institute for Radiological Sciences, Chiba, Japan. By use of modern imaging scans, the peak positions can be adjusted by changing the energy of the particle and arranged to cover the cancer. By landing as many peaks on the target as possible will reduce radiation in other areas.

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Essentially, far less radiation energy is deposited in the body - by a factor of two to 15 depending upon the anatomical site (see Figure 2). Charged particles allow:

- a marked reduction in radiation dose to normal tissues
- tumour dose escalation in clinically awkward situations, e.g. proximity of a cancer to the brain, spinal cord, kidney, bowel etc.
- a reduced risk of radiation-induced cancer in later life - especially important to children and young adults.

The small UK cyclotron at Clatterbridge was the first hospital-based proton therapy unit in the world for the treatment of ocular melanoma, using only four treatments in successive days. Over 2,000 patients have been treated with high eye retention rates.

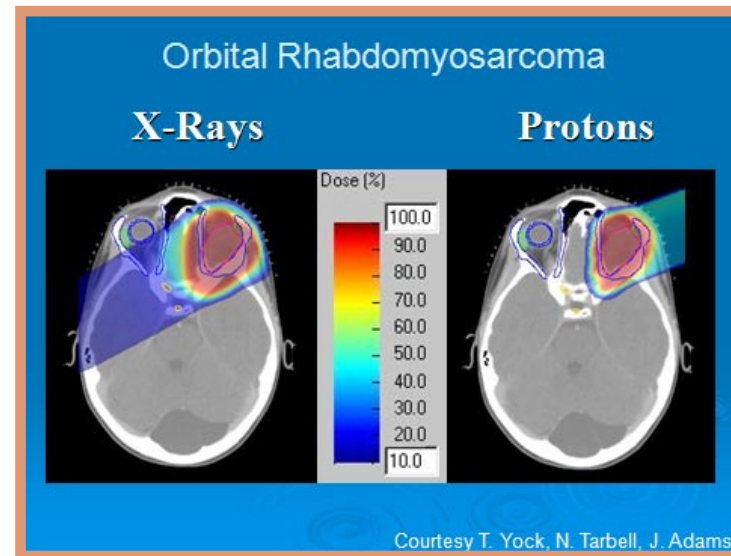


Figure 2: Example of proton therapy for a rare orbital tumour in a child at Massachusetts General Hospital, Boston, USA. The X-ray comparison shows how that beam deposits radiation dose to a much wider area, with consequent risks of future toxicity such as bilateral blindness.

There is a rapid expansion in proton and ion facilities in most advanced countries. The UK has been slow to develop plans for proton and ion beam therapy, but is expanding its budget for referral of a very limited number of patients abroad.

continued on next page >>>

▶ See following pages for the latest additions to NHS Evidence - cancer

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continued from front page

>>> Some of the many reasons for this include:

● **Cost.** Special cyclotrons or synchrotron accelerators are required to accelerate charged particles. Heavy and expensive gantries are used to bend the beam around a patient.

● **Evidence base.** The rationale for particle therapy is the improved radiation dose distribution based on the reliable predictions of physics. Many authorities regard these as being so impressive that randomised controlled studies are unnecessary for ethical reasons. Other medical doctors demand published reports of efficacy from countries that possess particle beams. The UK is unable to contribute data for cancers deeper than the eye.

A large research and development portfolio surrounds particle therapy, including cost reduction by:

● Use of fewer treatments. In Japan, lung and primary liver cancers are treated with only one exposure, and four treatments are used for prostate patients.

● Development of smaller and cheaper accelerators and gantries by British scientists engaged in Research Council funded projects.

Soon there will be 12 Japanese Centres, six in Germany, around 20 in the USA, with smaller numbers in Austria, Italy, France and Switzerland. These will concentrate on cancers that are difficult to treat with x-rays and those usually treated by radical surgery. Pioneering clinical results show equal survival rates, but far less morbidity than surgery or standard radiotherapy. Also, because of reduced bone marrow irradiation with particles, chemotherapy toxicity appears to be less severe.

Future demands for 'kinder radiotherapy' using particles are likely to increase with public awareness and especially if the medical evidence base improves.

FURTHER READING

Brada M, Pijls-Johannesma M, De Ruyscher D, Proton therapy in clinical practice: current clinical evidence. *J Clinical Oncology*, 2007; 25, 965-80.

Schultz-Ertner D & Tsujii H. Particle radiation therapy using proton and heavier ion beams. *J Clin Oncol* 2007; 25, 953-64.

Jones B. Personal View: The potential advantages of charged particle radiotherapy using protons or light ions. *Clinical Oncology [Royal College of Radiologists]*, 2008;20, 555-563.

Suit H, Kooy H, Trofimov A, Farr J, Munzenrider J, DeLaney T, Loeffler J, Clasie B, Safai S, Paganetti H. Should positive phase III clinical trial data be required before proton beam therapy is more widely adopted? No. *Radiother Oncol*. 2008, 86(2):148-53.

Useful website: Particle Therapy Co-Operative Group (PTCOG) <http://ptcog.web.psi.ch/>

New content:

All cancers

What are the unmet supportive care needs of people with cancer? A systematic review. *Support Care Cancer*. 2009. [Epub ahead of print]

Increased risk of high-grade dermatologic toxicities with radiation plus epidermal growth factor receptor inhibitor therapy. *Cancer*. 2009;115:1286-99.

The psychosocial impact of recurrence on cancer survivors and family members: a narrative review. *Journal of Advanced Nursing*. 2009 65(4), 724-736.

Preferences of cancer patients regarding communication of bad news: a systematic literature review. *Jpn J Clin Oncol*. 2009;39:201-16.

Homeopathic medicines for adverse effects of cancer treatments. *Cochrane Database of Systematic Reviews* 2009, Issue 2.

Publication outcomes of phase II oncology clinical trials. *Am J Clin Oncol*. 2009. [Epub ahead of print]

Breast cancer

Breast cancer seeding associated with core needle biopsies: a systematic review. *Maturitas*. 2009. 20;62:113-23.

Return to work of breast cancer survivors: a systematic review of intervention studies. *BMC Cancer*. 2009; 9:117.

Breast cancer sentinel node identification and classification after neoadjuvant chemotherapy-systematic review and meta analysis. *Acad Radiol*. 2009;16:551-63.

A systematic review of FDG-PET in breast cancer. *Med Oncol*. 2009. [Epub ahead of print]

NHS Evidence - cancer keeps its collections up to date.

These are some of the latest additions. Items in blue are 'Editor's pick' highlighted by Dr Chris Alcock, our Clinical Lead.

NHS Evidence - cancer has not performed in-depth appraisal for the systematic reviews and meta-analyses but has applied rigorous methods to select them.

We recommend that a full appraisal is completed using the appropriate tools provided by the Centre for Evidence-Based Medicine.

Post-operative radiotherapy for ductal carcinoma in situ of the breast. *Cochrane Database of Systematic Reviews* 2009, Issue 1.

Gabapentin for the treatment of hot flashes in women with natural or tamoxifen-induced menopause: a systematic review and meta-analysis. *Clin Ther*. 2009;31:221-35.

Central nervous system

Endoscopic pituitary surgery: a systematic review and meta-analysis. *J Neurosurg*. 2009. [Epub ahead of print]

Brain metastases. *Clin Evid (Online)*. 2009.

Localized BCNU chemotherapy and the multimodal management of malignant glioma. *Curr Med Res Opin*. 2009;25:149-60.

Endocrine

Adjuvant radiotherapy for thymic epithelial tumors: a systematic review and meta-analysis. *Ann Thorac Surg*. 2009;87:1641-7.

Annual Evidence Update (AEU)

An Annual Evidence Update (AEU) presents the incidence of new high-quality research evidence during a specific time period. The aim is to 'fill the gaps' between major guidelines or systematic reviews. They provide an opportunity to highlight significant new evidence that has emerged in the preceding year and to provide commentaries where possible to interpret or put that evidence into the context for current clinical practice.

The AEU on Oesophago-gastric cancer was published in June.

New content: continued

Gynaecological cancer

p16(INK4a) immunostaining in cytological and histological specimens from the uterine cervix: a systematic review and meta-analysis. *Cancer Treat Rev.* 2009;35:210-20.

Brachytherapy for cervix cancer: low-dose rate or high-dose rate brachytherapy – a meta-analysis of clinical trials. *J Exp Clin Can Res* 2009. 28:47

Increased ovarian cancer risk associated with menopausal estrogen therapy is reduced by adding a progestin. *Cancer.* 2009;115:531-9.

Ovarian cancer (advanced). *Clin Evid (Online)* 2009.

Haematology

Rituximab maintenance for the treatment of patients with follicular lymphoma: systematic review and meta-analysis of randomized trials. *J Natl Cancer Inst.* 2009;101:248-55.

Beneficial and harmful effects of anthracyclines in the treatment of childhood acute lymphoblastic leukaemia: a systematic review and meta-analysis. *Br J Haematol.* 2009;145:376-88.

Head and neck

Predictive value of tumor thickness for cervical lymph-node involvement in squamous cell carcinoma of the oral cavity: a meta-analysis of reported studies. *Cancer.* 2009;115:1489-97.

Meta-analysis of impaired vocal cord mobility as a prognostic factor in T2 glottic carcinoma. *Arch Otolaryngol Head Neck Surg.* 2009;135(5):479-86.

Treatment and follow-up of oral dysplasia - A systematic review and meta-analysis. *Head Neck.* 2009. [Epub ahead of print]

Lower GI

Colon cancer: preventive agents and the present status of chemoprevention. *Expert Opin Pharmacother.* 2009;10:211-9.

Second-line chemotherapy in advanced and metastatic CRC Cochrane Database of Systematic Reviews, Issue 2, 2009.

Patient satisfaction with colonoscopy: A literature review and pilot study, *Can J Gastroenterol.* 2009;23:203-9.

Updated systematic review and meta-analysis of randomized clinical trials on the role of mechanical bowel preparation before colorectal surgery, *Ann Surg.* 2009;249:203-9.

Lung

Lung cancer, *Clin Evid (Online).* 2009. pii: 1504

Endobronchial ultrasound-guided transbronchial needle aspiration for staging of lung cancer: A systematic review and meta-analysis. *Thorax.* 2009 18. [Epub ahead of print]

Musculoskeletal

Prognostic factors in localized extremity osteosarcoma: A systematic review, *Eur J Surg Oncol.* 2009 19. [Epub ahead of print]

Paediatric

Influenza vaccination in children being treated with chemotherapy for cancer. Cochrane Database of Systematic Reviews 2009, Issue 2.

Burnout, psychiatric morbidity, and work-related sources of stress in paediatric oncology staff: a review of the literature. *Psychooncology.* 2009 18. [Epub ahead of print]

Side-effects of treatment

A review of quality assessment of the methodology used in guidelines and systematic reviews on oral mucositis, *Journal of Clinical Nursing,* 18, 3–12.

Efficacy and Safety of Modafinil in the Treatment of Cancer-Related Fatigue (April). *Ann Pharmacother.* 2009;43:721-5. [Epub 2009 Mar 24.]

Skin

Solar ultraviolet radiation and skin cancer. *Occup Med (Lond).* 2009; 59: 828.

Tissue biomarkers for prognosis in cutaneous melanoma: A systematic review and meta-analysis, *J Natl Cancer Inst.* 2009 1;10:452-74. [Epub 2009 Mar 24.]

Upper GI

Surgery versus radical endotherapies for early cancer and high grade dysplasia in Barrett's oesophagus. Cochrane Database of Systematic Reviews 2009, Issue 2.

Systematic review: photodynamic therapy for unresectable cholangiocarcinoma. *J Hepatobiliary Pancreat Surg.* 2009. [Epub ahead of print]

Chemoradiotherapy in the management of locally advanced pancreatic carcinoma: a qualitative systematic review. *J Clin Oncol.* 2009; 27: 2269-77

Urology

Use of classical and novel biomarkers as prognostic risk factors for localised prostate cancer: a systematic review. *Health Technology Assessment.* 2009; 13:1-219.

The Updated EAU Guidelines on Muscle-Invasive and Metastatic Bladder Cancer. *Eur Urol.* 2009. [Epub ahead of print]

Prostate cancer and driving occupations: could whole body vibration play a role? *Int Arch Occup Environ Health.* 2009; 82: 551-6.

Treatment of metastatic renal cell carcinoma. *Cancer Chemother Pharmacol.* 2009;64:11-25