

Abstract Selection

1H magnetic resonance spectroscopy in the investigation of intractable epilepsy. Gadian, D. G., Connelly, A., Duncan, J. S., Cross, J. H., Kirkham, F. J., Johnson, C. L., Vargha-Khadem, F., Neville, B. G., Jackson, G. D. Radiology and Physics Unit, Institute of Child Health, London, England. *Acta Neurologica Scandinavica Supplement* (1994) Vol. 152, pp. 116–21.

We have been using proton magnetic resonance spectroscopy (1H MRS) in the investigation of adults and children with intractable epilepsy. Spectra were obtained from 2 × 2 × 2 cm cubes in the medial region of the temporal lobe, and were analyzed on the basis of signals from N-acetylaspartate (NAA), creatine + phosphocreatine (Cr), and choline-containing compounds (Cho). In comparison with control subjects, the epilepsy patients as a group show significant reductions in the NAA signal and in the NAA/Cho + Cr ratio, with increases in the Cho and Cr signals. The reduction in NAA is interpreted in terms of neuronal loss or damage, while the increase in Cr and Cho signals may be a reflection of reactive astrocytosis. Author.

Another family with tricho-rhino-phalangeal syndrome type III (Sugio-Kajii syndrome). Nagai, T., Nishimura, G., Kasai, H., Hasegawa, T., Kato, R., Ohashi, H., Fukushima, Y. Division of Pediatrics, Tokyo Metropolitan Kiyose Children's Hospital, Japan. *American Journal of Medical Genetics* (1994) February 1, Vol. 49 (3), pp. 278–80.

Tricho-rhino-phalangeal syndrome Type III (TRPS III) is a newly defined genetic entity. Only nine patients in a family and one sporadic patient have been reported. We add another family in which four individuals in three generations are affected with this autosomal dominant trait. Although they manifested short stature, sparse hair, 'pear-shaped' nose, and cone-shaped epiphyses, sharing these findings with TRPS Type I, the presence of a severe form of generalized shortness of all phalanges and metacarpals, and the absence of mental deficiency and exostoses in this family distinguish the disorder from the TRPS Types I and II. Their manifestations are quite similar to those of the patients reported as TRPS III (Sugio-Kajii syndrome). Author.

A cephalometric and electromyographic study of upper airway structures in the upright and supine positions. Pae, E. K., Lowe, A. A., Sasaki, K., Price, C., Tsuchiya, M., Fleetham, J. A. University of British Columbia, Department of Clinical Dental Sciences, Vancouver, Canada. *American Journal of Orthodontics and Dentofacial Orthopedics* (1994) July, Vol. 106 (1), pp. 52–9.

Obstructive sleep apnea (OSA) is characterized by recurrent upper airway obstruction during sleep, usually in the supine position. To investigate the relationship between upper airway size and genioglossus (GG) muscle activity, upright and supine cephalograms were obtained in 20 OSA patients and 10 symptom-free control subjects. Tongue electromyographic (EMG) recordings were obtained with surface electrodes, and pressure transducers were placed in the 10 symptom-free controls. The tongue cross-sectional area increased 4.3 per cent ($P < 0.05$), and the oropharyngeal area decreased 36.5 per cent ($P < 0.01$) when the OSA patients changed their body position from upright to supine. No changes were observed in the tongue area, but soft palate thickness increased ($P < 0.01$) when the control subjects changed from the upright to the supine position. Furthermore, the oropharyngeal cross-sectional area decreased 28.8 per cent ($P < 0.01$) despite a 34 per cent increase ($P < 0.05$) in resting GG EMG activity. Posterior tongue pressure increased 17 per cent ($P < 0.05$) with the change from upright to supine. On the basis of these findings, we propose that body posture has a substantial effect on upper airway structure and muscle activity. This postural effect should be taken into account when assessing upper airway size in the erect posture (conventional cephalography) and in the supine position (computed tomography). The vertical and anteroposterior position of the tongue and its relationship to airway size may be more important than soft palate size in the pathogenesis of OSA. Author.

A study of nasal respiratory resistance and craniofacial dimensions in white and West Indian black children. Jones, A. G., Bhatta, S. King's College School of Medicine and Dentistry, Department in Orthodontics, London, United Kingdom. *American Journal of Orthodontics and Dento-facial Orthopedics* (1994) July, Vol. 106 (1), pp. 34–9.

Two studies have shown that there are morphologic differences in the nasopharynx between the major racial groups. This investigation was conducted to see whether these morphologic differences affected nasal respiration. Twenty-two West Indian and 24 white children (mean age of 13 years 11 months) were studied to examine the relationship between nasorespiratory function and nasopharyngeal and dentofacial structure. The nasorespiratory function was measured in terms of nasal respiratory resistance, NRR, (Pascals/cm³ per second), both by anterior and posterior methods, with a computerized rhinomanometer. Nasopharyngeal structure was described in terms of cephalometric variables. The West Indian cephalometric profile generally conformed to its existing description in the literature including prognathic jaws and bimaxillary proclination; in addition, the West Indians were found to have a greater bony nasopharyngeal width (posterior nasal spine-basion) and shallower nasopharyngeal roof angle (posterior nasal spine-hormion-basion). All rhinomanometric measurements were significantly lower in the West Indian group, especially when posterior rhinomanometry was used. The correlation coefficients between the cephalometric and the rhinomanometric measurements were statistically significant but low. In addition, the measure of mandibular prognathism (angle SNB) was also found to be significantly correlated with the nasorespiratory resistance. Author.

Motor signs of wakefulness during general anaesthesia with propofol, isoflurane and flunitrazepam/fentanyl and midlatency auditory evoked potentials. Schwender, D., Faber-Zullig, E., Klasing, S., Poppel, E., Peter, K. Institute for Anaesthesiology, University of Munich, Germany. *Anaesthesia* (1994) June, Vol. 49 (6), pp. 476–84.

Auditory evoked potentials have been used as an indicator of awareness. In the present study we combined epidural analgesia with three techniques of general anaesthesia. Motor signs of intra-operative wakefulness were documented and assessed along with cardiovascular changes and with midlatency auditory evoked potentials. Thirty patients undergoing elective laparotomy were studied as follows: first continuous epidural analgesia was used in all patients to block painful sensation to the level of T5. Intravenous general anaesthesia was induced with propofol (2.5 mg kg⁻¹ b.w., group 1, $n = 10$), thiopentone (5 mg kg⁻¹ b.w., group 2, $n = 10$) or etomidate (0.2 mg kg⁻¹ b.w., group 3, $n = 10$) and maintained with a propofol (3–5 mg kg⁻¹, group 1), isoflurane (0.4–0.8 Vol percentage, group 2), flunitrazepam and fentanyl (0.005 mg kg⁻¹ b.w.) bolus injection every 20 to 30 s (group 3). Heart rate and arterial pressure were recorded continuously. Purposeful movements of the limbs, eye-opening or other movements as well as coughing were documented as motor signs of intra-operative wakefulness. Auditory evoked potentials were recorded in the awake state, after induction and during maintenance of general anaesthesia. Motor signs of intra-operative wakefulness occurred statistically significantly more often in the patients of the flunitrazepam/fentanyl group than in those of the propofol and isoflurane group. There was no correlation between wakefulness and cardiocirculatory parameters. In the awake patients midlatency auditory evoked potentials had high peak to peak amplitudes and a periodic waveform. Author.

The influence of nasal obstruction and its relief on oxygen saturation during sleep and the early postoperative period. Serpell, M. G., Padgham, N., McQueen, F., Block, R., Thomson, M. Department of Anaesthesia, Ninewells Hospital and Medical School, Dundee, Scotland. *Anaesthesia* (1994) June, Vol. 49 (6), pp. 538–40. Nasal obstruction causes abnormal breathing patterns during sleep

which often result in hypoxaemia. We studied the effect of nasal obstruction on arterial oxygen saturation in 20 healthy patients undergoing elective surgery which required bilateral nasal packing. Ten patients were subject to complete nasal obstruction while the remaining half had the obstruction relieved by the insertion of nasal cannulae. We found that nasal obstruction did not have any detrimental effect on the already low incidence of oxygen desaturation. There was no effect of the cannulae on the degree or frequency of hypoxaemia, although they did appear to improve the quality of sleep during the first postoperative night. They were more comfortable by day than simple packing alone and no adverse effects were observed. author.

Brainstem auditory evoked response changes following electro-acupuncture therapy in chronic pain patients. Kumar, A., Tandon, O. P., Dam, S., Bhattacharya, A., Tyagi, K. K. Department of Anaesthesiology and Critical Care, University College of Medical Sciences, Delhi, India. *Anaesthesia* (1994) May, Vol. 49 (5), pp. 387–90.

Brainstem auditory evoked responses were recorded in 17 patients with chronic pain who had been given electro-acupuncture therapy. The absolute peak latencies of waves I to V, and interpeak latencies and amplitudes of waves I and V were analyzed before electro-acupuncture and compared with values obtained during electro-acupuncture and 5 min after its termination after one, five and 10 sittings. At these sittings the intensity of pain was recorded with the help of a 100 mm visual analogue scale. Each patient had 10 sittings given on alternate days. The absolute peak latencies of waves I, II, and III were delayed significantly ($P < 0.05$) after 5 and 10 sittings and amplitudes of wave V decreased significantly ($P < 0.05$) after 5 and 10 sittings. Visual analogue scores also decreased significantly ($P < 0.01$) during these sittings. It was established that before and after 10 sittings of electro-acupuncture, there was a significant positive correlation between visual analogue scores and the amplitude of wave V ($P < 0.01$). There was a negative correlation between visual analogue scores and absolute peak latencies of wave III at 1, 5 and 10 sittings, suggesting that there is a definite interaction between the electro-acupuncture neural mechanism and the generators of brainstem auditory evoked responses in the lower brainstem. Author.

Effects of the cervical collar on cerebrospinal fluid pressure. Raphael, J. H., Chotai, R. Department of Anaesthetics, Pilgrim Hospital, Boston, Lincolnshire. *Anaesthesia* (1994) May, Vol. 49 (5), pp. 437–9.

We investigated the hypothesis that cervical collars might compress the internal jugular veins and raise intracranial pressure in head-injured patients. In a randomized, single-blind, crossover study of nine patients scheduled for elective spinal anaesthesia the cerebrospinal fluid pressure in the lumbar subarachnoid space was measured with and without a 'Stifneck' cervical collar applied. There was a significant elevation of cerebrospinal fluid pressure in seven of the patients studied when the cervical collar was applied ($P < 0.01$). This preliminary study raises the possibility that immobilization of the cervical spine with the 'Stifneck' cervical collar may, by raising the intracranial pressure, contribute to secondary neurological injury in head-injured patients in whom intracranial compliance is already reduced. Author.

PRAD-1 (CCND1)/cyclin D1 oncogene amplification in primary head and neck squamous cell carcinoma. Callender, T., El-Naggar, A. K., Lee, M. S., Frankenthaler, R., Luna, M. A., Batsakis, J. G. Department of Otolaryngology, Baylor College of Medicine, Houston, Texas. *Cancer* (1994) July 1, Vol. 74 (1), pp. 152–8.

BACKGROUND. Abnormalities in chromosome 11q13 regions have been frequently found in head and neck squamous carcinoma. Recent studies indicate that the PRAD-1 (also CCND1), which encodes cyclin D1, is a putative oncogene that is an important component of this region. **METHODS.** DNA was extracted from 32 snap-frozen specimens from primary head and neck squamous carcinomas. DNA from peripheral blood lymphocytes, normal mucosa, and salivary gland tissue were used as controls. A genomic DNA probe containing the first exon of PRAD-1 was used for hybridization with specimen DNAs by the Southern technique. A 5.6 kb genomic DNA probe of immunoglobulin heavy chain was used as an internal standard for assessing PRAD-1 amplification. **RESULTS.** Eleven (34.4 per cent) squamous carcinoma specimens showed PRAD-1 amplification (2- to 10-fold). Although no significant statistical correlation among amplification status, grade stage, and DNA ploidy was observed in this small cohort, amplification was

more noted in high grade, high stage, and aneuploid tumors. A highly statistical correlation between PRAD-1 amplification and proliferative activity was noted ($P > 0.001$). **CONCLUSION.** The results of this study indicate that PRAD-1 amplification appears to be a late event in the tumorigenesis of head and neck carcinoma and is associated often with a subset of aggressive tumors and high proliferation neoplasms. Author.

Onset and duration of inhibition of ipratropium bromide nasal spray on methacholine-induced nasal secretions. Wagenmann, M., Baroody, F. M., Jankowski, R., Nadal, J. C., Roecker-Cooper, M., Wood, C. C., Naclerio, R.M. Johns Hopkins University School of Medicine, Department of Medicine (Division of Clinical Immunology), Baltimore, MD 21224. *Clinical and Experimental Allergy* (1994) March, Vol. 24 (3), pp. 288–90.

We performed a randomized, double-blind, placebo-controlled cross-over study with two different concentrations of ipratropium bromide (Atrovent) nasal spray to evaluate its onset and duration of inhibition. Twenty-four subjects with perennial rhinitis participated in the trial. Fifteen minutes to 12 hours after administration of ipratropium bromide (42 or 168 micrograms/nostril) or placebo nasal spray, methacholine challenges were performed and nasal secretion weights measured. After placebo administration the effect of methacholine remained unchanged over the 12-h period. Both the 42 and 168 micrograms/nostril doses significantly inhibited the nasal hypersecretions induced by methacholine challenge within 15 min of treatment ($P < 0.05$). The 168 micrograms dose of ipratropium bromide continued to significantly reduce secretion weights through 6 h, but the effectiveness of the 42 micrograms dose disappeared within 3 h. In addition to having a longer duration, the 168 micrograms/nostril dose produced approximately twice the inhibitory effect of the 42 micrograms dose. Author.

Sonographic appearance of branchial cysts. Reynolds, J. H., Wolinski, A. P. Department of Radiology, Russells Hall Hospital, Dudley, West Midlands. *Clinical Radiology* (1993) August, Vol. 48 (2), pp. 109–10.

Branchial cysts are developmental anomalies arising from remnants of the foetal branchial apparatus. Two patients in whom the presence of a branchial cyst was confirmed at surgery had undergone pre-operative neck ultrasound examination. In each case the cysts showed a characteristic uniform low echogenicity. Recognition of this appearance allows prompt and appropriate further investigation and treatment. Author.

Reversibility of brain stem evoked potential abnormalities in abstinent chronic alcoholics: one-year follow-up. Cadaveira, F., Corominas, M., Rodriguez-Holguin, S., Sanchez-Turet, M., Grau, C. Departamento de Psicología Clínica a Psicobiología, Universidad de Santiago de Compostela, Spain. *Electroencephalography and Clinical Neurophysiology* (1994) June, Vol. 90 (6), pp. 450–5. Brain-stem auditory evoked potentials (BAEPs) were studied in 34 chronic alcoholics who had been abstinent for one year, and in age- and sex-matched control subjects. The patients were examined three times, at one month, five months and one year after the start of the abstinence treatment. At one month of abstinence the alcoholics showed differences with respect to controls in the peak V latency ($P < 0.01$), and in the III–V ($P < 0.01$) and I–V ($P < 0.01$) intervals. After one year of abstinence a significant improvement in the V ($P < 0.01$), III–V ($P < 0.01$) and I–V ($P < 0.01$) parameters was recorded. The most notable development was in the 5–12 month period, with shortening in V latency ($P < 0.01$) and in the I–V interval ($P < 0.01$); in the first five months there was only shortening in the III–V interval ($P < 0.01$). This improvement was also indicated by a decrease in the number of patients with BAEP parameter abnormalities. The recovery of the functions impaired by chronic alcohol consumption after one year of abstinence was incomplete, although the tendency was towards normalization. Author.

Flow cytometric quantification of the proliferation-associated nuclear antigen p105 and DNA content in advanced head and neck cancers: results of RTOG 91-08. Fu, K. K.,¹ Hammond, E.,² Pajak, T. F.,³ Clery, M.,³ Scott Doggett, R. L.,⁴ Byhardt, R. W.,⁵ McDonald, S.,⁶ Cooper, J. S.⁷ ¹Department of Radiation Oncology, University of California, San Francisco, CA; ²Department of Pathology, LDS Hospital, Salt Lake City, UT; ³Radiation Therapy Oncology Group Statistical Unit, Philadelphia; ⁴Radiation Oncology Center, Sacramento, CA; ⁵Department of Radiation Oncology, Medical College of Wisconsin, Milwaukee, WI; ⁶Depart-

ment of Radiation Oncology, University of Rochester, NY; ⁷New York University-Tisch Hospital, New York, NY. *International Journal of Radiation Oncology, Biology and Physics* (1994) Vol. 29, no. 4, pp. 661–671.

PURPOSE: p105 is a proliferation-associated nuclear antigen which identifies proliferating but not resting cells. The objectives of this Radiation Therapy Oncology Group (RTOG) protocol (91-08) were: (1) to correlate tumour proliferative potential estimated using the p105 assay and deoxyribonucleic acid (DNA) analysis with treatment outcome in patients irradiated for advanced squamous cell carcinoma of the head and neck; and (2) to evaluate the potential of p105 labelling indices as a predictive assay. **METHODS AND MATERIALS:** Paraffin blocks of pretreatment biopsies of the primary tumor or metastatic neck nodes of patients with Stage III or IV squamous cell carcinoma of the head and neck treated with radiotherapy alone in three previous RTOG protocols (79-13, 79-15 and 83-13) were retrospectively obtained. From these paraffin blocks, areas of tumor were selected based on histological examinations and sectioned. Nuclei suspensions were then prepared and processed for p105 antibody and DNA staining and subsequent flow cytometric quantification of p105 labelling indices and DNA content and correlation with local-regional control and survival. **RESULTS:** Paraffin blocks of tumor biopsies from 148 out of a total of 598 eligible patients were available. Of these, 143 were analyzable. The median and (range) of p105 labelling index (LI-C), p105 labelling index of cells in S phase (LI-S), and p105 antigen density (AD) were: 66.6 (3.85–99.5), nine (1.55–36), and 93.2 (7.4–628.5), respectively. Deoxyribonucleic acid was diploid in 67 (47 per cent), aneuploid in 22 (15 per cent) and mixed aneuploid/diploid in 54 (38 per cent) patients. There was a strong correlation between AD and DNA ploidy. Antigen density was above median in 91.5 per cent of the aneuploid or mixed aneuploid/diploid tumors, but only in 8.5 per cent of the diploid tumors. Patients with aneuploid or mixed aneuploid/diploid tumors had significantly greater local-regional failures than patients with diploid tumors ($P = 0.0180$). Those with p105 LI-C below the median or p105 AD above the median also had significantly greater local-regional failures ($P = 0.0500$ and $P = 0.0167$, respectively). Patients with p105 AD below the median had significantly better survival than those above the median ($P = 0.0444$), although there was no significant difference in survival with respect to DNA ploidy or p105 LI-C. Multivariate analyses showed that T-stage ($P = 0.0001$) and p105 AD ($P = 0.0044$) were significant prognostic factors for local-regional control, and T-stage ($P = 0.0080$), N-stage ($P = 0.0021$), primary site ($P = 0.0110$), and p105 AD ($P = 0.326$) were significant prognostic factors for survival. **CONCLUSION:** These results suggest that flow cytometric quantitation of the proliferation-associated nuclear antigen p105 and DNA content of pretreatment tumor biopsies may be a potentially useful predictive assay in patients irradiated for advanced squamous cell carcinomas of the head and neck.

The study of tumoral, radiobiological, and general health factors that influence results and complications in a series of 448 oral tongue carcinomas treated exclusively by irradiation. Pernot, M.,* Malissard, L.,† Hoffstetter, S.,* Luporsi, E.,‡ Peiffert, D.,* Aletti, P.,† Kozminski, P.,§ Bey, P.† *Department of Brachytherapy, †Department of Radiation Therapy, ‡Department of Bio-Statistics, § Department of Head and Neck Tumors, Centre Alexis Vautrin, 54500 Vandœuvre-les-Nancy, France. *International Journal of Radiation, Oncology, Biology and Physics* (1994) Vol. 29, No. 4, pp. 673–679.

PURPOSE: Our aim was to study the different factors that influence the results and complications in a series of 448 carcinomas of the oral tongue treated from January 31 1972 to December 31, 1986, by brachytherapy (Br) ± neck dissection (181 cases) or combination of external beam irradiation and brachytherapy (EBI + Br) (267 cases). **METHODS AND MATERIALS:** The patients distribution (TNM classification 1979) was: 125 T₁, 186 T₂, 128 T₃, 9 T₄, 78 per cent N₀, and 22 per cent N+. We used guide gutter or plastic tubes technique (Paris system dosimetry). Results at five and 10 years are: local control 68 and 64 per cent, locoregional control 58 and 53 per cent, specific survival 45 and 39 per cent, and overall survival 44 and 27 per cent. **RESULTS:** In the univariate analysis for local control (LC) and overall survival (OS), we considered the tumoral factors. At five years, the LC for T₁, T₂, T₃ are 93, 65 and 49 per cent, and the OS 69, 41 and 25 per cent, respectively ($P < 0.002$). The lesions of the undersurface of the tongue have a better LC (77 per cent) than other localizations (64 per cent) ($P = 0.02$). For general factors, the

index of general health condition, age and sex were not significant for LC, but proved significant for OS ($P = 0.01$). Significant radiobiological factors: the safety margin (expressed by the ratio treated surface on tumoral surface ≥ 1.2) is significant for LC and OS. This is the same if the interval between EBI and Br is ≤ 20 days. Neither the dose rate, the space between the sources, the total dose, nor Br dose were significant, but the last two were adapted according to the infiltration. In the univariate study for grade 2 and 3 complications (tissue and bone), the surface treated ($> 12 \text{ cm}^2$), and the dose rate $> 0.7 \text{ Gy/h}$ were significant. **CONCLUSION:** The multivariate study showed that the small size of the lesion is the most important factor for local control, with brachytherapy alone for T₁T₂N₀ and the number of days between EBI and brachytherapy ≤ 20 days. For the complications, the most important factors are the total dose $> 80 \text{ Gy}$ and a treated surface $> 12 \text{ cm}^2$.

Salvage irradiation by brachytherapy of velotonsillar squamous cell carcinoma in a previously irradiated field: results in 73 cases. Peiffert, D.,^{1,2} Pernot, M.,¹ Malissard, L.,³ Aletti, P.,⁵ Hoffstetter, S.,^{1,2} Kozminski, P.,³ Luporsi, E.,⁴ Dartois, D.,⁴ Bey, P.² ¹Brachytherapy Department, ² Radiotherapy Department, ³Head and Neck Department, ⁴Bio-Statistics Department, ⁵Radio-Physics Department, Centre Alexis Vautrin, 54500 Vandœuvre-les-Nancy, France. *International Journal of Radiation, Oncology, Biology and Physics* (1994) Vol. 29, No. 4, pp. 681–86.

PURPOSE: The salvage brachytherapy performed in patients presenting velotonsillar carcinoma in a previously irradiated field is evaluated in terms of local control, complications and survival. **METHODS AND MATERIALS:** Between 1976 and 1990, 73 patients presenting with velotonsillar squamous cell carcinoma in a previously irradiated area were treated at Centre Alexis Vautrin with brachytherapy alone using an ¹⁹²Ir Implant (afterloading technique) with curative intent. According to the UICC 1987 TNM classification, there were 45 T₁N₀, 20 T₂N₀, one T₃N₀, one T₃N₁, and six T₄N_x. **RESULTS:** The five-year actuarial local control for T₁N₀ and T₂N₀ are 80 per cent and 67 per cent respectively. The regional relapse rate was 10 per cent in both groups. Grade 2 complications occurred in 13 per cent of patients and these were neither related to the volume treated nor the dose rate. There were no Grade 3 or 4 complications. The five-year specific survival is 64 per cent, with a plateau after the fifth year, but the five-year overall survival is only 30 per cent. Forty-two per cent of the patients in this series died from another carcinoma. All but two of these were related to continued alcohol and tobacco intoxication. **CONCLUSION:** We conclude that brachytherapy alone (60 Gy) is optimal treatment for patients presenting with velotonsillar carcinoma in a previously irradiated field. The greatest challenge is the screening of these patients and the prevention of subsequent head and neck cancers. Recognizing the fact that these patients are at high risk for subsequent malignancies of upper aerodigestive tract, lung and esophagus, close surveillance is necessary for: (a) early diagnosis and prompt treatment; and (b) development of prevention strategies of field cancerization.

Radiotherapy for nasopharyngeal carcinoma: shielding the pituitary may improve therapeutic ratio. Sham, J., Choy, D., Kwong, P. W. K., Cheng, A. C. K., Kwong, D. L. W., Yau, C. C., Wan, K. Y., Au, G. K. H. Radiotherapy and Oncology Service, Queen Mary Hospital, Pokfulam, Hong Kong. *International Journal of Oncology, Biology and Physics* (1994) Vol. 29, No. 4, pp. 699–704.

PURPOSE: Nasopharyngeal carcinoma (NPC) is well known for its invasiveness and erosion of the base of the skull is not uncommon. Before the advent of computed tomography, the evaluation of the base of the skull was by plain radiography. Because of the low sensitivity of these investigations, traditional teaching has included the sphenoid sinus in the volume of irradiation. Increase in longevity of patients allows the manifestation and documentation of the long-term sequelae of irradiating the hypothalamic-pituitary axis and the temporal lobes. This study is an attempt to evaluate whether the hypothalamic-pituitary axis can be shielded from the target volume in a proportion of NPC patients. **METHODS AND MATERIALS:** One hundred and fifty-two NPC patients with no evidence of erosion of the base of the skull and sphenoid, nor extension to the nasal fossa and ethmoid sinuses were randomized to receive standard radiotherapy covering the whole sphenoid sinus or radiotherapy using a modified technique that shields the pituitary and the anterior part of the hypothalamus. This modified technique also shields a large part of the lower temporal lobes that are otherwise covered by standard treatment portals. The characteristics and treatment of the two sub-

groups of patients were otherwise comparable. **RESULTS:** At a median follow-up of 31.5 months, the tumor control between the two subgroups of patients were comparable ($P = 0.3928$). However, eight of the 71 patients in the unshielded group had developed symptomatic neuroendocrine complications, while none of the other group did ($P = 0.0061$). Two patients developed secondary hypothyroidism, one patient developed oligomenorrhoea associated with raised prolactin, and five patients developed temporal lobe necrosis. **CONCLUSIONS:** The protective effect on neuroendocrine complication of this shield was demonstrated at median follow-up of 31.5 months, and the local control was not jeopardized. Modification of treatment technique as presently described, which is applicable to one-third of NPC patients to improve the therapeutic ratio, is recommended for general use.

The choice of treatment of single brain metastasis should be based on extracranial tumor activity and age. Noordijk, E. M.,¹ Vecht, C. J.,² Haaxma-Reiche, H.,³ Padberg, G. W.,⁴ Voormolen, J. H. C.,⁵ Hoekstra, F. H.,⁶ Tans, J. Th. J.,⁷ Lambooi, N.,⁸ Metsaars, J. A. L.,⁹ Wattendorff, A. R.,¹⁰ Brand, R.,¹¹ Hermans, J. ¹Departments of ¹Radiation Oncology, ²Neurology, ³Neurosurgery and ⁴Medical Statistics, University Hospital Leiden; ⁵Department of Neurology, Dr Daniel den Hoed Cancer Center, Rotterdam; ⁶Department of Neurology, University Hospital Groningen; Departments of ⁷Radiotherapy and ⁸Neurology, Westeinde Hospital, The Hague; Departments of ⁹Neurosurgery, ¹⁰Radiotherapy and ¹¹Neurology, Leyenburg Hospital, The Hague, The Netherlands*. *International Journal of Radiation Oncology, Biology and Physics* (1994) Vol. 29, No. 4, pp. 711–717.

PURPOSE: To determine if in patients with single brain metastasis the addition of neurosurgery to radiotherapy leads to lengthening of survival or to better quality of life. **METHODS AND MATERIALS:** From 1985 to 1990, 66 patients with single brain metastasis from a solid tumor were entered in a randomized trial of neurosurgery plus radiotherapy vs radiotherapy alone. Patients were stratified for lung cancer vs other sites of cancer and for progressive vs stable systemic cancer. Radiotherapy was given to the whole brain by a novel scheme of two fractions of 2 Gy per day for a total dose of 40 Gy in two weeks, to obtain a relatively high total dose and short overall time, with minimal risk of late damage to normal tissue in long-term survivors. **RESULTS:** In the whole group of 63 evaluable patients, both with lung cancer as with other tumors, the combined treatment led to a better duration of survival (median 10 vs six months; $P = 0.04$). The largest difference between both treatment arms was observed in patients with inactive extracranial disease (median 12 vs seven months; $P = 0.02$). Patients with active extracranial disease had an equal median survival of only five months, irrespective of given treatment. Age proved to be a strong and independent prognostic factor: patients older than 60 years had a hazard ratio of dying of 2.74 ($P = 0.003$) compared with younger patients. Following treatment, most patients remained functionally independent until a few weeks before death. In the majority of patients the cause of death was systemic tumor progression. **CONCLUSION:** Patients with single brain metastasis and with controlled or absent extracranial tumor activity should be treated with surgery and radiotherapy, especially when they are younger than 60 years. For patients with progressive extracranial disease, radiotherapy alone seems to be sufficient. The accelerated radiotherapy scheme of 40 Gy in two weeks to the whole brain is tolerated well and should also be considered for patients in a good performance status with surgically unaccessible single metastasis or even with multiple brain metastases.

Preliminary results of a pilot study using WR-2721 before fractionated irradiation of the head and neck to reduce salivary gland dysfunction. McDonald, S.,* Meyerowitz, C.,† Smudzin, T.,* Rubin, P.* *Departments of Radiation Oncology and †Clinical Dentistry, University of Rochester Medical and Dental Center, Rochester, NY. *International Journal of Radiation, Oncology, Biology and Physics* (1994) Vol. 29, No. 4, pp. 747–754.

PURPOSE: Based on *in vivo* evidence of radioprotection of the salivary glands using WR-2721, a pilot study was undertaken to determine the feasibility, toxicity, and salivary function of patients receiving WR-2721, while undergoing radiation therapy to the head and neck. **METHODS AND MATERIALS:** Patients undergoing radiation therapy for cancer of the head and neck were eligible if the major salivary glands received more than 45 Gy. WR-2721 was administered over 6 min IV, 10–15 min prior to each dose of radiation five times per week. Saliva was collected and measured prior to radiation therapy, weekly during radiation therapy, one month post-

radiation therapy, and every three months thereafter. Flow rates of unstimulated whole saliva, stimulated whole saliva, and stimulated parotid saliva were measured using standard techniques. ^{99m}Tc salivary scintiscans were performed prior to radiation therapy, one month post radiation therapy and every three months thereafter. Nine patients are presently enrolled on the first dose level (100 mg/min²) of this study. Eight completed per protocol, two with minor decreases of total WR-2721 doses. Two patients progressed with distant metastases soon after completion of therapy. All available data are included in the analysis. Median follow-up for all patients is 18 months. **RESULTS:** Flow rates of unstimulated whole saliva decreased significantly during radiation therapy reaching 5.6 per cent of baseline at nine months post radiation therapy, subsequently recovering to 20 per cent of baseline, then remaining stable over time. Stimulated whole salivary flow rate similarly decreased during radiation therapy and reached its nadir (11 per cent of baseline) at three months post radiation therapy, improving to 27 per cent of baseline by two years. The stimulated parotid flow rate decreased during radiation therapy to 1.4 per cent of pretreatment levels. Significant recovery took place six months post radiation therapy and by 18 months values had recovered to 54 per cent of baseline. ^{99m}Tc salivary scintiscans confirmed this rebound of parotid function post radiation therapy. Toxicity was minimal with the exception of one patient who received only 27 per cent of the planned total drug dose due to grade 3 hypotension after the eighth treatment. No recovery of salivary function has been seen in this patient; flow rates remain zero in all three areas tested 21 months after radiation. **CONCLUSIONS:** Administration of WR-2721 prior to each dose of radiation was feasible and without significant toxicity at 100 mg/m². Salivary gland function improved over time after completion of radiation, particularly the parotid. Future directions include escalation of WR-2721 dose to 200 mg/m² and then 300 mg/m², and a Phase III randomized trial will be undertaken once the optimal dose is established.

Pitch perception for different modes of stimulation using the cochlear multiple-electrode prosthesis. Busby, P. A., Whitford, L. A., Blamey, P. J., Richardson, L. M., Clark, G. M. Department of Otolaryngology, University of Melbourne, Parkville, Victoria, Australia. *Journal of the Acoustical Society of America* (1994) May, Vol. 95 (5 Pt 1), pp. 2658–69.

Numerical estimations of pitch were obtained from nine postlinguistically deafened adults using the 22-electrode cochlear implant manufactured by Cochlear Pty Ltd. A series of electrodes on the array were stimulated using three modes of stimulation: Bipolar (BP), common ground (CG), and monopolar (MONO). In BP stimulation, an electric current was passed between two electrodes separated by one electrode for eight patients and two electrodes for one patient. In CG stimulation, a single electrode was activated and the other electrodes on the array were connected together to serve as the return path for the current. In MONO stimulation, an electric current was passed between a single electrode and the most basal electrode on the array. Pitch estimations were generally consistent with the tonotopic organization of the cochlea. There was a marked reversal in pitch for electrodes in the middle of the array using CG stimulation for three patients. A reduced range of pitch using MONO stimulated was recorded for patients where the most basal electrode was internal to the cochlea. There were also individual differences in pitch estimations between the three modes of stimulation for most patients. The current levels required to elicit threshold (T) and comfortable listening (C) levels were, in general, higher for BP stimulation than for CG stimulation and were lowest for MONO stimulation. For CG stimulation, there was a tendency for T and C levels to be higher for electrodes in the middle of the array than at the basal or apical ends. For MONO stimulation, T and C levels uniformly increased in an apical to basal direction for the majority of patients. There was no consistent pattern in T and C levels for BP stimulation. The size of the range of usable hearing using CG stimulation tended to be similar to that using BP stimulation and was usually higher than that using MONO stimulation. Author.

Relationships between regional ventilation and vascular and extravascular volume in supine humans. Brudin, L. H., Rhodes, C. G., Valind, S. O., Jones, T., Jonson, B., Hughes, J. M. Medical Research Centre, Cyclotron Unit, Royal Postgraduate Medical School, Hammersmith Hospital, London, UK. *Journal of Applied Physiology* (1994) March, Vol. 76 (3), pp. 1195–204.

With the use of positron emission tomography, alveolar ventilation (VA), lung density, and pulmonary blood volume (VB) were measured regionally in eight nonsmokers in the supine posture and

one nonsmoker in the prone posture during quiet breathing in a transaxial thoracic section at midheart level. Regional values of alveolar volume (VA) and extravascular tissue volume (VEV) were derived from the inherent relationships between different compartments in the lung. Ratios proportional to gas volume (VA/VEV) and ventilation (VA/VEV) per alveolar unit, respectively, were calculated. No differences between right and left lung were found. Variations in the vertical direction could explain approximately 65 per cent of the total within-group variation in VA, VB and ln (VA), whereas the corresponding value for horizontal variation was only three to nine per cent (right lung, supine subjects). Similar gravitational gradients were found in the single prone subject. There was a significant linear correlation between VA and ln (VA). When VA and VEV are related to a given number of alveolar units (VEV), the data are consistent with a linear relationship between VA/VEV and VEV, indicating that ventilation might be explained by the elastic properties of lung tissue according to Salazar and Knowles (*Journal of Applied Physiology* 1964; **19**: 97–104). Regional VB was closely associated with the gradient of regional alveolar volume (VA/VEV) (by virtue of weight of blood and competition for space) and therefore, indirectly, closely associated with the vertical gradient of ventilation. Author.

Long-term evaluation of discectomy of the temporomandibular joint. Takaku, S., Toyoda, T. Department of Oral and Maxillofacial Surgery, Saitama Medical School, Japan. *Journal of Oral and Maxillofacial Surgery* (1994) July, Vol. 52 (7), pp. 722–6; discussion 727–8.

A clinical and radiographic survey was conducted with 39 patients (39 joints) who had undergone discectomy of the temporomandibular joint between 1965 and 1974 and whose cases had been followed for an average of 20 years after surgery. There were three males and 36 females, ranging in age from 16 to 70 years (average, 33 years) at the time of surgery. Masticatory disorders, arthralgia, limitation of condylar movement, and trismus were the chief symptoms, and clicking and crepitus were present in six and two patients, respectively. Plain radiography showed osteoarthritic changes such as osteophyte formation or lipping on the condyles of eight joints. Arthrography showed disc perforations and peridiscal adhesions in 27 patients, and displacement of the disc in eight. All discs were totally extirpated and condylar shaves were performed in eight patients who had disorders such as osteophytes, exostoses, or lipping on the condyles. In follow-up examinations, 37 patients had no pain, but mild arthralgia was noted occasionally in two patients. Postoperatively, no patients experienced subjective masticatory disorders; 38 patients were able to open their mouth more than 35 mm, and crepitus was heard in only two joints. Plain radiography showed bony changes on the condyles and eminences of all joints. From this long-term follow-up study it is concluded that discectomy is a useful operation for treatment of severe disc pathology causing pain and functional disturbance in the temporomandibular joint. Author.

Alveolar bone resorption: a histologic study comparing bone turnover in the edentulous mandible and iliac crest. Devlin, H., Sloan, P., Luther, F. Department of Restorative Dentistry, University Dental Hospital of Manchester, UK. *Journal of Prosthetic Dentistry* (1994) May, Vol. 71 (5), pp. 478–81.

The extent of bone formation and resorption in alveolar and basal mandibular bone was measured in 17 edentulous individuals. For comparison, samples of iliac crest bone were also collected because this bone is often used for standard site assessment of skeletal measures of bone turnover. The specimens were processed for undercalcified resin histology. The results indicated extensive bone resorption at the periosteal surface of the alveolar crest, with little evidence of subsequent osteoid formation. Endosteal osteoid formation did occur, which tended to maintain the thickness of the cortical bone at the alveolar crest. Mandibular basal bone displayed a remodelling pattern similar to that seen in the iliac crest. Author.

A prospective investigation of the long-term auditory-neurological sequelae associated with bacterial meningitis: a study from Vanuatu. Carroll, K. J., Carroll, C. Lenakel Hospital, Tanna, Vanuatu. *Journal of Tropical Medicine and Hygiene* (1994) June, Vol. 97 (3), pp. 145–50.

During the period August 1988–July 1991 all cases of bacterial meningitis admitted to Lenakel Hospital on the island of Tanna in Vanuatu were followed. During this period there were 83 cases of purulent meningitis giving an annual incidence of 134 per 100,000 population. There were 13 deaths during the acute illness phase (CFR = 15.7 per cent). Of the 70 survivors 65 (93 per cent) were suc-

cessfully followed for a mean duration of 17.5 months. When grouped by severity of illness there was no significant difference in the mean age, duration of symptoms or sex of the patients. At the time of discharge 31.5 per cent had auditory-neurological abnormalities. During follow-up 35 per cent of the survivors were found to have one or more auditory-neurological sequelae. Hearing loss was the most frequent abnormality occurring in 32.2 per cent of the study group. Of those with auditory-neurological sequelae 39 per cent were judged to have severe disabilities likely to impair their ability to live independently. A statistically significant association was found between the severity of the illness at presentation and the risk of auditory-neurological sequelae. Meningitis caused by *Streptococcus pneumoniae* was associated with the highest incidence of sequelae and that caused by *Hemophilus influenzae* type b with the lowest. There was no association with sex or age group. Strategies to reduce the mortality and morbidity from bacterial meningitis in developing countries are briefly discussed. Author.

Effects of indoor environmental factors on respiratory systems of children. Guneser, S., Atici, A., Alparslan, N., Cinaz, P. Cukurova University Medical Faculty, Department of Pediatrics, Adana, Turkey. *Journal of Tropical Pediatrics* (1994) April, Vol. 40 (2), pp. 114–6.

Effects of indoor environmental factors on children's respiratory system and pulmonary function tests were investigated in this study. A total of 617 primary school children aged between 9–12 years were included. A standard questionnaire, which includes questions about respiratory symptoms and illness, indoor environmental determinants, family history of respiratory diseases, and smoking habits of the parents, was sent to homes of all children and information was obtained from parents. Children with a family history of asthma, bronchitis, or other chest troubles suffered morning and day/night coughs, shortness of breath, wheezing and asthma, bronchitis, or pneumonia more frequently. Children whose mothers smoked complained of blocked-runny nose and sinusitis more frequently. Pulmonary function levels were diminished in passive smokers and in children whose houses were heated by a wood-burning stove. As a result, passive smoking, using a wood-burning stove for heating, and family history of respiratory diseases are to be considered risk factors for the respiratory system. Author.

Cortical localization of temporal lobe language sites in patients with gliomas. Haglund, M. M., Berger, M. S., Shamseldin, M., Lettich, E., Ojemann, G. A. Department of Neurological Surgery, University of Washington, Seattle. *Neurosurgery* (1994) April, Vol. 34 (4), pp. 567–76; discussion 576.

In a series of 40 patients undergoing an awake craniotomy for the removal of a glioma of the dominant hemisphere temporal lobe, cortical stimulation mapping was used to localize essential language sites. These sites were localized to distinct temporal lobe sectors and compared with 83 patients without tumors who had undergone language mapping for the treatment of intractable epilepsy. In patients with and without temporal lobe gliomas, the superior temporal gyrus contained significantly more language sites than the middle temporal gyrus. Both patient populations also had language sites anterior to the central sulcus in the superior temporal gyrus (12–16 per cent). The patients without tumors had significantly more language sites in the superior temporal gyrus, compared with the superior temporal gyrus of patients with temporal lobe tumors. Multiple variables were studied for their effect on preoperative and postoperative language deficits and included age, sex, number of language sites, histology, size of the tumor, and the distance of tumor resection margins from the nearest language site. The distance of the resection margin from the nearest language site was the most important variable in determining the improvement in preoperative language deficits, the duration of postoperative language deficits, and whether the postoperative language deficits were permanent. If the distance of the resection margin from the nearest language site was >1 cm, significantly fewer permanent language deficits occurred. Cortical stimulation mapping for the identification of essential language sites in patients with gliomas of the dominant hemisphere temporal lobe will maximize the extent of tumor resection and minimize permanent language deficits. Author.

Preservation of hearing in operations on acoustic tumors: an alternative to recording brain stem auditory evoked potentials. Moller, A. R., Jho, H. D., Jannetta, P. J. Department of Neurological Surgery, University of Pittsburgh School of Medicine, Pennsylvania. *Neurosurgery* (1994) April, Vol. 34 (4), pp. 688–92; discussion 692–3.

The monitoring of auditory function by recording brain stem auditory evoked potentials in patients undergoing removal of acoustic tumors is hampered by the small amplitude of the brain stem auditory evoked potentials. Because several thousands of responses must be added, it takes several minutes to obtain an interpretable record. Recordings done directly from the exposed VIIIth nerve have much higher amplitudes, and, therefore, interpretable responses can be obtained after only a few responses have been added. However, it is difficult to place the recording electrode in an optimal position and the electrode may interfere with the removal of the tumor. In this report, we show that evoked potentials from the cochlear nucleus, which can be recorded by placing an electrode in the lateral recess of the IVth ventricle, have a large amplitude, and that the electrode placed in this way does not interfere with the removal of the tumor. This way of monitoring, therefore, yields interpretable responses within 15 to 20 seconds, or less, and makes it possible to detect injuries to the entire intracranial portion of the VIIIth nerve, just as brain stem auditory evoked potentials do, but 20 to 50 times faster. Author.

Glomus tumors of the skull base: combined use of MR angiography and spin-echo imaging. Vogl, T. J., Juergens, M., Balzer, J. O., Mack, M. G., Bergman, C., Grevers, G., Lissner, J., Felix, R. Department of Radiology, University of Berlin, Clinic Rudolf Virchow, Germany. *Radiology* (1994) July, Vol. 192 (1), pp. 103–10. **PURPOSE:** To evaluate the use of magnetic resonance (MR) angiography in the diagnosis of glomus tumors of the skull base. **MATERIALS AND METHODS.** In forty patients with pulsatile tinnitus, spin-echo (SE) images, single sections, and maximum intensity projections from gradient-echo sequences, including arterial MR angiography and MR venography, were evaluated for tumor detection. Interpretations by two independent observers were correlated with findings from histologic examination, digital subtraction angiography, computed tomography, and clinical follow-up. **RESULTS:** Glomus tumors were detected near the tympanic plexus ($n = 8$) and close to the superior ($n = 8$) and inferior ($n = 1$) ganglia of the vagus nerve. Sixteen of 18 proved tumors were detected with SE images alone. Although four high-lying jugular bulbs were misinterpreted as tumor due to similar signal intensity, combined evaluated allowed differentiation between tumor and sinus blood flow in all cases. **CONCLUSION:** The authors recommend combined SE imaging and MR angiography for ruling out tumor in patients with pulsatile tinnitus. Author.

Suppression of odorant responses by odorants in olfactory receptor cells. Kurahashi, T., Lowe, G., Gold, G. H. Monell Chemical Senses Center, Philadelphia, PA 19104. *Science* (1994) July 1, Vol. 265 (5168), pp. 118–20.

Odorants activate an inward current in vertebrate olfactory receptor cells. Here it is shown, in receptor cells from the newt, that odorants can also suppress this current, by a mechanism that is distinct from inhibition and adaptation. Suppression provides a simple explanation for two seemingly unrelated phenomena: the anomalously long latency of olfactory transduction and the existence of an 'off response' at the end of a prolonged stimulus. Suppression may influence the perception of odorants by masking odorant responses and by sharpening the odorant specificities of single cells. Author.

An experimental study of tracheal reconstruction using a freed piece of the right bronchus. Murakami, S., Sato, H., Yokoi, K., Tanezuka, N., Hayashi, Y., Shimizu, J., Watanabe, Y. Department of Surgery, Kanazawa University School of Medicine, Japan. *Thoracic and Cardiovascular Surgery* (1994) April, Vol. 42 (2), pp. 76–80.

An experimental study of tracheal reconstruction using a separate piece of bronchus was performed in six dogs. After right upper lobectomy, a five-cartilage-ring length of the trachea extending from five cartilage rings above the carina was circumferentially resected; the right bronchus was transected just below the carina and above the second carina to provide the piece of bronchus, which was then interposed between the distal end of the upper trachea and the proximal end of the lower trachea by end-to-end anastomoses. One stoma type carinal reconstruction (an anastomosis between the carina and the right intermediate bronchus) was performed. After completion of the airway reconstruction, the anastomotic site was wrapped with an omental flap. One dog died 14 days after operation due to anorexia and weakness, the necropsy in this dog revealed severe ischemic change of the interposed bronchus and ulcer formation at the stump of the upper bronchus. The other five dogs survived the operation. Bronchoscopically, the findings for the interposed free bronchus revealed severe ischemic change immediately after the operation, but almost normal findings were observed four to five weeks after the operation. The clinical relevance of this method of tracheal reconstruction is discussed. Author.