netic study was performed in 8 consecutive patients of our phase II trial of the modified ELF regimen. Included were 8 males, median age 56 years (range 39–66), four gastric and four cardia carcinoma, two following resection (partial resection type Bilroth II, proximal gastric resection), two local recurrence after resection, and four with the primary tumour *in situ*. Sites of metastatic disease were the liver in 4, lymph nodes in 5 and malignant peritonitis in 1 patient.

In the pharmacokinetic study, etoposide was given on day 1 at a dose of 50 mg intravenously in 10 min, on day 3 one capsule of 50 mg orally, and from day 4 to day 15 50 mg twice a day. In following courses, etoposide was administered at a fixed dose of 2x50 mg days 1–15. In addition, leucovorin (300 mg/m^2) and 5-fluorouracil (500 mg/m^2) were given intravenously at the same dosage as in the original ELF regimen [5]. The oral bioavailability, area under the curve (AUC) orally/AUC intravenously, was 58% ± 16. This finding is similar to the 57% reported by D'Incalci [6] in 1982, and not greatly different from the dose-dependent findings in the recent report of Hande[2].

In conclusion, bioavailability of orally administered etoposide did not seem to be grossly impaired in patients with a pathologically or partially resected stomach.

1. Pinkerton CR, Dick G, Aherne GW. 24-hour plasma etoposide profile after oral and intravenous administration in children. *Eur J Cancer* 1993, **29A**, 1479–1481.
2. Hande KR, Krozely MG, Greco FA, Hainsworth JD, Johnson DH. Bioavailability of low-dose oral etoposide. *J Clin Oncol* 1993, **11**, 374–377.
3. Slevin Ml, Joel SP. Prolonged oral etoposide in small cell lung cancer. *Ann Oncol* 1993, **4**, 529–532.
4. Comis RL. Oral etoposide in oncology: an evolving role. *Ann Oncol* 1992, **14** (suppl.), A3.
5. Wilke H, Preuser P, Fink U, *et al.* High dose folinic acid/etoposide/5-fluorouracil in advanced gastric cancer—a phase II study in elderly patients or patients with cardiac risk. *Invest New Drugs* 1990, **8**, 65–70.
6. D'Incalci M, Farina P, Sessa C, *et al.* Pharmacokinetics of VP16-213 given by different administration methods. *Cancer Chemother Pharmacol* 1982, **7**, 141–145.

European Journal of Cancer Vol. 30A, No. 3, pp. 421–422, 1994.

0959–8049/94 $6.00 + 0.00

Why Don't We Use a "Cavalieri"?

J. K. D. Bentzen

IN PHASE II and III trials with chemotherapy, it is common practice to use the terms CR (complete response), PR (partial response), NC (no change) and PD (progressive disease) in evaluation of treatment response. The WHO definitions of these terms are based on a two-dimensional assessment of tumour size [1]; the largest diameter of the tumour is measured, and multiplied by the diameter perpendicular to it. PD is defined as a 25% increase in size as defined above, and PR is defined as at least a 50% reduction in tumour size. Assuming that tumours are spheroid in shape, and that they grow or shrink equally in all three dimensions, the actual changes in tumour volume corresponding to the WHO criteria are 40% for PD and 65% for PR. In other words, a treatment is not stopped until the tumour has grown by 40%, and a response is not classified as 'PR' until the tumour is reduced to 35% of its initial size. Any changes between these are classified as 'NC'. This way of measuring tumour size is rather inadequate but, nevertheless, we still use the WHO criteria for evaluation, in spite of having access to three dimensional information such as computed tomography (CT) or magnetic resonance (MR) scans.

I would like to suggest a very simple and more exact method of determining tumour volumes from CT scans. The method is borrowed from the relatively new scientific field of stereology, but the principle was originally described by the sixteenth century (1598–1647) Italian mathematician Cavalieri [2]. According to the principle of Cavalieri the volume, V, of an object can be determined by cutting it into parallel slices separated by a known distance, t, summing up the areas of the cross sections and multiplying by t. Then, $V = t \times \sigma$ area is a close approximation to the true volume.

The only condition is that the first section must be placed at random in the object. This principle is ideal when you have a tumour visualised on CT slides. The precise distance between the slides is well known (usually 1.0 cm) and the tumour area from each slide can very easily be estimated. A sheet of transparent film with marked, regularly arranged reference points, each point a known area [a(p)] (corrected for the magnification of the scans), is superimposed randomly over each of the scans containing the tumour. On each scan, the number of points within the tumour are counted (σp). The size of the tumour (v) can then be estimated from the following simple equation: $V(\text{tumour}) = t \times a(p) \times \sigma p$. For example, if the t = 1.0cm, a(p) =0.25 cm^2 and σp = 77 points then $V(\text{tumour}) = 1.0\ \text{cm} \times 0.25\ \text{cm}^2 \times 77 = 19.25\ \text{cm}^3$.

The precision of the method is very much dependent on the irregularity of the object measured. For tumours that tend to be more or less spheroid in shape, approximately 75 points should be counted in no less than five slides to give an unbiased estimate of the true volume, with a precision better than 5% [1–6].

If the tumour is less than 5 cm, perpendicular to the scanning plane, a distance between slices less than 1.0 cm must be used in order to have at least five scans containing tumour, but this should not cause any problems. Once familiar with the method, counting the necessary points takes minutes. With this level of precision, waiting until the tumour volume has grown by 40% before stopping the treatment of a patient with an ineffective drug will no longer be necessary since 10% will probably be sufficient. Similarly, waiting until the tumour volume is reduced to 35% before classifying a PR will not be necessary, and many of the NCs encountered in chemotherapy trials can be categorised as either PRs or PDs.

Furthermore, if this method becomes generally accepted and a specified precision for reporting results is agreed upon, then comparison of results from different centres will be more meaningful. The method is easy, precise and unbiased and I strongly recommend it be implemented.

Correspondence to J.K.D. Bentzen at the Fasanvaenget 107, 2980 Kokkedal, Denmark.
Received 23 Aug. 1993; accepted 6 Sep. 1993.

1. WHO. *WHO Handbook for Reporting Results of Cancer Treatment.* Geneva, World Health Organisation, 1979.
2. Gundersen HJG, Bendtsen TF, Korbo L, *et al.* Some new, simple and efficient stereological methods and their use in pathological research and diagnosis. *APMIS* 1988, **96**, 379–394.
3. Gundersen HJG, Jensen EB. The efficiency of systematic sampling in stereology and its prediction. *J Microsci* 1987, **147**, 229–263.
4. Pakkenberg B. Postmortem study of chronic scizophrenic brains. *Br J Psychiat* 1987, **151**, 744–752.
5. Pakkenberg B, Boesen J, Albeck M, Gjerris F. Unbiased and efficient estimation of total ventricular volume of the brain obtained from CT-scans by a stereological method. *Neuroradiology* 1989, **31**, 413.
6. Regeur L, Pakkenberg B. Optimizing sampling designs for volume measurement of components of human brain using a stereological method. *J Microsci* 1988, **155**, 113–121.
7. Sørensen FB, Braendgaard H , Christiansen AO, Bojsen-Møller M, Reske-Nielsen E. Stereological estimates of nuclear volume and other quantitative variables in supratentorial brain tumours. Practical technique and use in prognostic evaluation. *J Neurooncol* 1991, **10**, 253.