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Multi-Centre Trials with PET: Physical Prerequisites

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Quite frequently, quantitative results from different positron emission tomographs and from different institutions are merged in multi-centre studies. For quantitative evaluation it is not sufficient that lesions are just visible, they should also reflect true size and true activity concentration. A more advanced type of quantitative analysis creates parametrical images scaled in biological units, such as blood flow or glucose metabolic rate. This type of analysis in general is based on physiological models and requires dynamic acquisitions and the measurement of an input function stemming from blood samples.

The ability of an imaging device to reproduce truly regional tracer uptake in an image may be reduced to three basic demands:

1. A uniform tracer distribution in the object has to be imaged homogeneously;
2. It is imperative that even slight regional variations in tracer uptake are reflected in very small lesions;
3. There must be a linear relationship between regional signal in the image and the corresponding activity concentration in the object.

In reality these ideal conditions are not fulfilled. The deviations between ideal and real world are described by performance parameters and call for proper corrections such as for dead time, random coincidences, attenuation, scatter, and recovery effects as well as for appropriate quality control of the instrument.

In general, all quantitative procedures ultimately require that the scanner be calibrated and that the peripheral devices (i.e. dose calibrator and well counter) be cross calibrated to the scanner, preferably in terms of absolute activity. Calibration is the process of establishing the relationship between the measured count rate per volume and the true activity concentration. Calibration gains even more importance when data collected and analysed by different scanners and at different institutions are compared, typically when pooling patient data for multi-centre studies. The basic calibration method is similar for all dedicated PET scanners and has to be performed for each mode of data acquisition. However, procedures differ depending on scanner manufacturer and type. Ideally, calibration consists of measuring a phantom containing a known and homogeneous activity concentration, preferably determined with the on-site dose calibrator. For cross calibration of the well counter, an aliquot of the phantom content has to be withdrawn. In practice, a manufactured calibration phantom is used in most cases, containing a certified activity of the long-lived positron emitter Ge-68 in a solid matrix, thus preventing withdrawal of a sample to check either the dose calibrator or the well counter. The volume of matrix carrying the activity is not certified, leaving uncertainty about activity concentration. In this case, the recommended procedure is to cross calibrate the matrix volume against another cylindrical phantom containing a solution of a short-lived positron emitter, such as F-18, of known activity and volume. The activity is determined using the on-site dose calibrator, and the well counter is then checked using a sample from this phantom. This type of calibration procedure clearly depends on the accuracy of the on-site dose calibrator. However, if the same dose calibrator is used to determine the amount of activity injected into the patient, any small deviation in accuracy will be cancelled out, provided that the deviation is constant and the complete cross calibration procedure has been followed, including nuclide-specific corrections for branching ratio and decay. The procedural accuracy of the method that is actually used depends on the accuracy of the corrections applied; especially those for attenuation and scatter, which in turn may be dependent on the physical principle of correction and the software used.

In quantitative PET, the image count rate per volume (representing tissue activity concentration) is related to the injected dose (e.g., determination of standardized uptake values) and to the blood activity concentration (physiologic modelling). Therefore, careful cross calibration between the PET scanner, dose calibrator, and well counter is essential.

The calibration accuracy of the scanners between institutions can be examined by comparing phantom data. When the accuracy is found to be degraded, the source of error should be investigated. To facilitate analysis of errors and pooling of data from different institutions the absolute accuracy of the dose calibrators should be also checked using a set of certified standards. The calibration chain starts with the dose calibrator, whose accuracy is therefore of fundamental importance. Quality control alone, although a prerequisite for operation of PET scanners, does not guarantee the accuracy of scanner calibration.

For clinical multi-centre studies relying on quantitative analysis of PET data, the calibration of scanners must be carefully checked beforehand and reflect the status of the devices at that time. Permanent monitoring by the participating institutions is needed to maintain this condition.

But even if the PET scanner is in a good operational state, the necessary corrections are applied to a sufficient degree of accuracy, and calibration and cross-calibration is perfect, the problem of recovery and its correction remains, i.e. the relationship between image activity concentration and true object activity concentration and its dependency from object size and reconstructed spatial resolution. The problem of recovery correction is quite complex and extends well beyond the topic of calibration, but at least its existence should be kept in mind when quantifying small lesion data.

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