身體組成測定的質量控制

Quality control in body composition measurements

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The principles of quality control (QC) are not new; they have always been with mankind. At the most fundamental level QC can be defined as a state of mind in which we continually strive to analyse what we are doing in order to produce a 'product' which our peers will judge to be 'better'. Paradoxically, this simple concept is expressed in many different ways within the multi-disciplinary team that makes up a body composition laboratory and very careful discussion is needed to ensure uniformity of technique and results. The situation is made even more difficult by the large range of equipment and techniques that are now available for the measurement of body composition. It is necessary to have a detailed understanding of the equipment and techniques and to have good communication within the group of workers. Good communication is essential to ensure that all members of the group have a clear understanding of the relevant guidelines and principles of QC and measurements, and to ensure that they are applied consistently throughout all the work of the laboratory. A detailed understanding of the equipment is necessary in order to define and implement simple tests that will monitor the most sensitive or troublesome features without imposing an undue burden upon the operator. There is a need for such tests to be automated as much as possible and, in general, there is a need for a more professional approach to the analysis of error and its propagation throughout an experiment. Inter comparisons of results between centres is a logical, but generally difficult requirement and some of the problems that arise would be simplified if equipment designs were more standardized. Finally, all these requirements need to be achieved within an environment that is continually changing with respect to the aims of the laboratory and the funding bodies.

Introduction

The origins of quality control (QC) go back to the roots of our modern civilization and, to quote the most obvious example, it is impossible to imagine the building projects of the ancient Egyptians, Greeks, South Americans and Chinese without what we would now call a highly developed QC programme. Great publicity has been given to the application of QC (and TQM) within the manufacturing sector since the Second World War and significant advances have occurred there, but the basic principles are inherent in any human endeavour in which we attempt to produce a 'product' that will please other people. Indeed, the basic principle of QC is that we have an attitude of mind, an approach to our work, which causes each of us to continually analyse what we are doing in order to produce a 'product' which our peers will judge to be 'better'.

This definition is in the first person to imply even more clearly that QC is a responsibility of all staff at all times. The word 'product' may seem inappropriate for a body composition laboratory/project, but it was carefully chosen; the product is the data from the laboratory and it must be reliable, objective and subject to a minimum of limitations. As in all science, it is the peer group that is the judge of the success of a QC programme not the individual(s) doing the work; to argue otherwise would be socially anachronistic. It is not clear from this definition where QC begins or ends although there is always room for improvement in any experiment. QC is generally limited to the data-gathering and data-analysis stages of the project and it is not applied to other aspects of the project, such as setting the aim.

Modern authors such as Feigenbaum[1] see QC virtually entirely within an industrial production setting and ignore other fields of endeavour, despite the fact that scientists (and many other professions) have been applying the principles of QC long before the invention of the continuously moving production line in 1913[2] and Deming's epic visits to post-war Japan[3]. QC has always been an inherent part of any scientific endeavour, but the stage is set for QC to assume a more prominent role in our body composition laboratories. There is an increasing number of laboratories competing with one another and QC will be seen as one measure of professionalism. At the same time, funding bodies are themselves becoming more professional and some are now requiring evidence of a suitable QC program as a condition of their grants; most laboratories would hardly be in a position to argue with the logic of such an approach.

There is an incredible range of techniques in use within laboratories for measuring percent fat, bio-impedance, total body nitrogen, total body potassium, bone mineral density as well as various laboratory assays for measuring water spaces, nitrogen balance, etc. There is also a large variety of equipment ranging from 'home-made' to commercial. This range of techniques and equipment is a barrier to the implementation of an overall QC program, because such a programme demands a clear understanding and documentation of these techniques, the procedures and the equipment itself. Sources of error must be understood and eliminated or controlled. Such understanding and control may require years of dedicated application before all the subtleties of a complex piece of equipment are discovered and understood. Purchasers may demand suitable QC programs as part of the package when ordering new equipment, but it is not always possible for a

manufacturer to supply such information. It is often more realistic for purchasers to work with the manufacturer in order to develop such a programme, especially if the equipment is being used in a new or different application. For these and other reasons it may take many years to establish a comprehensive QC program.

This review will concentrate on four of these techniques, viz anthropometry, total body nitrogen by in vivo neutron activation analysis, total body potassium by whole body counting and total body water by D_2O dilution. These are some of the major measurements currently undertaken in the laboratory at the Monash Medical Centre (MMC). Much of the discussion will concern precision and accuracy of the techniques; this is consistent with the theme of this paper since optimization of the precision and accuracy of a test is one of the main aims of a QC program.

Anthropometry

Two significant developments have occurred in recent years relating to the standardization of anthropometric measurements. The first is the publication of an Anthropometric Standardization Reference Manual by Lohman et al.[4] following from the decisions of the Airlie Consensus Conference in 1985. More recently, the WHO Expert Committee on Anthropometry[5] has formulated recommendations on appropriate reference data and simple methods for collecting and interpreting information. This work is directed towards Third World nations and the alleviation of malnutrition problems[6]. These standards will lead to more consistent data sets and help to eliminate the differences between centres that have hampered the intercomparison of data. Nevertheless, these are not the only standards that are used for anthropometry as shown by the review of Kerr[7] who describes the widespread use of the O-Scale technique in sports medicine.

Straightforward measurements of weight and height are the basis of our discipline, yet it is embarrassing how often we find inconsistencies in our recorded results. Perhaps this is one reason why some standards require that data entered manually into a computer must be checked by a second person if the laboratory is to receive accreditation. It is a very straightforward task to interface a set of electronic scales to a small computer and to automate the data collection, storage and reporting processes. This would eliminate various sources of error from the weight measuring and recording process. However, we can go further and routinely apply systematic tests to most of our data as it is being collected and/or entered into the computer. For example, height measurements might be compared when patients have visited more than once and flagged if they differ by more than a set amount. This check could conceivably reveal a number of possible problems.

Total body nitrogen

Total body nitrogen (TBN) is measured by counting the gamma rays that are emitted when ^{14}N is activated by a neutron. The prompt IVNAA technique is used at the MMC[8] and various other laboratories[9,10] for measuring TBN. Clinical experience at these centres confirms that it is a very useful and reliable test[11,12] and many details of the equipment have been investigated[13] at the various centres. TBN is one of the very few body composition measurements in which it is possible to make a direct measurement of the actual quantity required (assuming the protein = 6.25 × nitrogen). Various QC tests are undertaken daily on the equipment of the MMC, but the more interesting aspects concern the determination of precision and accuracy for this test.

All TBN measurements are relative to a phantom containing a urea solution. The precision of the TBN measurement is limited by the total number of nitrogen gamma rays counted from the patient, the background counts and, to a lesser extent, the counts from the urea phantom. The precision of each patient measurement can be calculated from these counts. Daily measurements are made on the urea and other phantoms and the variation from day to day has been used to calculate the precision of a patient measurement and so confirm that the equipment is stable and the above-mentioned calculation of precision is correct. These methods confirm that the MMC equipment is stable and that TBN can be measured in an adult with a precision of ±4% (sd). Most other laboratories achieve similar or better precision.

It is generally believed that the accuracy of TBN measurements is also well understood. When performing a TBN measurement, the neutron flux is not uniform throughout the patient; it is highest near the point that the neutron beam enters the patient and much lower on the opposite side[14]. Many laboratories employ neutron sources both above and below the patient in order to make the neutron flux more uniform. Even then, problems can arise because the nitrogen is not uniformly distributed throughout the patient's body, and Vartsky et al.[15] proposed that the hydrogen in the body be used as an internal standard. This reduces the error significantly, but it still assumes that the ratio of nitrogen-to-hydrogen is uniform throughout the body. A further problem arises because a fraction of the gamma rays that are being counted are absorbed within the patient's body before they can reach the detectors. All laboratories have undertaken phantom measurements to study these effects and most laboratories apply a small correction to their results depending mainly upon the patient's width. They generally claim that the accuracy for TBN measurements in adults is approximately ±4%. As a demonstration of their accuracy, most laboratories have performed measurements on pigs and/or meat samples; the results have then been compared with chemical analysis[16,17]. Other tests involve the use of phantoms measured at various laboratories[18]. Obese patients may well be regarded as a further test of these techniques and corrections, but Monte Carlo calculations by McGregor et al[19] have shown that surprisingly accurate measurements of TBN can be obtained with these methods. A recent report by Borovnicar et al.[20] demonstrates that consistent TBN measurements can be obtained in obese patients.

As a further test of the accuracy of the MMC facility, a group of 16 normal volunteers were measured[8] and good agreement was obtained with results from Toronto[21]. Subsequent measurements on a larger group of normal volunteers indicated that the Melbourne measurements are about 10% lower than the Toronto results[11]. Extensive testing in both laboratories has failed to show the cause for this discrepancy.

If there were a standard design for IVNAA equipment it would be simpler to share QC programs between laboratories. However, most IVNAA equipment has been designed locally and built on a very limited budget. To further complicate the situation, there are several different types of IVNAA equipment and the choice of equipment would depend on the particular interests of the laboratory. Mitra[22] has recently demonstrated the advantages of a design which employs fast neutron interactions; it measures total body carbon, nitrogen

and oxygen with a radiation dose that is lower than the dose in the Melbourne facility. Mitra's technique would be of interest in a laboratory specializing in energy studies, whereas the Melbourne method may be preferred in others because of its ability to measure chlorine as well as nitrogen. The Swansea[23] laboratory has yet another variation of the IVNAA principle. All of these different designs require immense effort to complete QC programs and such programs are expensive, especially if they involve tests designed to guarantee that measurements taken in one laboratory will agree with those from another laboratory employing a somewhat different technique.

The conclusions that can be drawn are that the corrections that are applied to the data are not as well understood as we might wish. Inter-laboratory comparisons may raise as many questions as they answer. When these inter-laboratory comparisons involve measurements on normal volunteers measured at both laboratories, they can be expensive and difficult to co-ordinate and they may not be as effective as phantoms for resolving the outstanding questions. The problems would be reduced if standardized equipment were used, but this would take attention away from the development of other novel techniques.

Total body potassium

Total body potassium (TBK) is measured by counting the gamma rays that are emitted when ^{40}K decays within the body. Most laboratories use large NaI detectors for counting the gamma rays. A shadow shield detector has been designed and constructed at the Monash Medical Centre[24]. It is based upon four 100 x 100 x 400 mm NaI detectors which are located within a large open-ended, steel box that provides shielding from the potassium in concrete and other building materials. The detectors are arranged two above and two below the patient. The patient lays on a bed which is moved slowly through the box in a 30 minute counting cycle. TBK is measured by comparing the number of counts from the patient with the counts from a water phantom that contains a known amount of potassium. As in the TBN measurement, some of the gamma rays are absorbed within the patient and a correction is necessary. The correction depends mainly upon the thickness of the patient; measurements have been performed on phantoms at the MMC to determine this correction.

The comments made above regarding precision and accuracy in the measurement of TBN apply to the measurement of TBK. The precision of the measurement is well understood and most physicists would claim to understand the accuracy quite well. When measuring TBK, it is possible to perform an absolute calibration using ^{42}K which is another radioactive isotope of potassium; when it decays it emits a gamma ray with an energy very similar to that of ^{40}K. Volunteers are given a known amount of ^{42}K and are then measured in the counter after a suitable equilibration time. These measurements have not been undertaken at the MMC because we decided to calibrate the counter using phantoms. Fenwick et al.[25] have reported on a series of measurements made on a set of phantoms that were measured at 10 whole body counters in the UK; they pointed out that the phantoms have advantages over the use of human volunteers.

The measurement of TBK is simpler in principle than that of TBN, but the range of equipment designs is far greater[24], and this adds to the difficulties when inter-laboratory comparisons are attempted. The measurement of obese patients presents another set of problems and our laboratory does not yet have a suitable technique for obese patients[26]. However, we are currently looking at methods of adapting this equipment for the measurement of infants.

Total body water

At the MMC the D_2O dilution method is used for the measurement of total body water (TBW) because D_2O is cheap, small amounts are non-toxic and it is not radioactive. TBW has been measured in many laboratories using tritiated water, but as reported by the Auckland group[10], this gives a radiation does of 0.2 mSv to the patient; there is no radiation dose with D_2O. There are many methods for measuring the concentration of D_2O in the plasma or saliva samples that are obtained from the patient. Blagojevic et al.[27] have shown that the use of a fourier transform infra-red spectrometer has several advantages over other methods. The equipment is substantially cheaper than either a mass spectrometer or nuclear magnetic resonance equipment. Compared with the older fixed filter infra-red method, purification of the serum samples by vacuum sublimation is not necessary, and water cooling of the sample holder is not required to avoid temperature drifts.

The skills required to maintain the spectrometer and to perform the analysis are very different to those required for the tests described above and it has taken several years to develop the expertise within the group to a level such that the technique is not dependent upon just one or two key personnel. Such delays are unavoidable when tests of this complexity are introduced. Optimum performance of the spectrometer is maintained by performing the QC tests recommended by the manufacturer, though experience is required to interpret the results from these tests and to perform the necessary adjustments. A high level of laboratory skills is also required for this test and the appropriate QC tests for this type of measurement are well described in several papers[27,28], including the use of standard solutions for the measurement of intra- and inter-assay variability. One of the major lessons to be drawn from working with this test is that the Body Composition Laboratory and the quality of its QC programme are very dependent upon the skills and experience of all the staff members and it is essential that policies be adopted to ensure that suitable expertise is acquired within the group and that the group is not dependent upon a single person.

Discussion and conclusion

There are actually very few papers in the open literature that discuss quality control in body composition measurements, although there are many that discuss precision and accuracy of various techniques[29]. In a paper such as this it would be very easy to under-rate the QC efforts of other laboratories and previous generations of workers. This would be a very distorted reading of the history of these measurements, but QC is an on-going challenge. Efforts must be made to make QC a routine part of all measurements so that reliable data and results will be obtained.

It is essential to have good communication between the various members of the group within a laboratory if an effective quality control program is to be maintained. It is not unusual to find variations in technique between people within a laboratory and it is necessary to implement review processes in order to ensure that significant differences are eliminated and techniques are standardized. These communication problems are made more difficult by the multi-disciplinary nature of many body composition research groups;

workers from different disciplines often have very different views of what is an appropriate technique and great care is necessary to produce the required cohesiveness within the group. One obvious method to assist this standardization is to prepare a Procedures Manual; the exercise of preparing such a document and then reviewing it within the group will raise many issues of quality control and standardization. A well-prepared Procedures Manual will be valuable when comparing procedures with other laboratories, and it will be of great assistance to other groups who are in the process of establishing new laboratories and/or projects.

Despite all of the high technology developments, simple anthropometric techniques are still the fundamental measurements of body composition analysis. Weight, height, body mass index, waist-to-hip ratio and skinfold measurements are vital determinants of health. Vast libraries of such data have been accumulated and entered manually into computers, but the technology exists now for these data to be automatically transferred from the measuring instruments to a computer. The automatic recording of such data would eliminate many transcription errors and save time. There is a need to address this problem so that laboratories will eliminate this source of error. When such measurements are made on-line, it will be possible to introduce simple consistency tests which will eliminate other sources of error and to implement some forms of on-line reporting.

When reviewing the literature concerning the precision and accuracy of measurements of TBN and TBK it is obvious that the precision of these measurements is well understood. Various studies have been undertaken to compare results from various centres; they do find significant differences, but very often the major factor contributing to these differences is the difference in estimates of the calibration factors. It is a time-consuming task to prepare these factors for each centre and the factors that are available depend upon the applications for which the equipment has been designed and used. The pressure to develop new techniques adds to these problems by diverting effort away from the established techniques. More inter-laboratory comparisons are required, but these need to be part of a well-planned experiment designed to investigate specific problems.

The measurement of body composition and its variations still present many challenges for physical scientists and other workers. However, the challenge is determined ultimately by the patients, the resources and the questions that need to be answered. The problems range from over-nutrition in high-technology environments to studies of normality and under-nutrition in Third World countries populated by many different ethnic groups. Irrespective of the setting, QC must continue to play a vital role in all experimental work and lead us to improve the quality of our data through a process of continual review.

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