Measurement of human energy expenditure

Valorisation

The relevance of human calorimetry and its current status.

Human Energy Expenditure is the single most important aspect of life, without this energy there is no life. For this reason, interest in the energy of living is as old as recorded science, starting with Plato in 360 B.C. and exponentially growing ever since physics allowed the measurements of this energy as demonstrated for mammals by Lavoisier and Laplace in 1780.
It was at the start of the 20th century that research into Human Energy Expenditure became a well understood science, and during the course of the 20th century a vast and solid body of information on food, food-composition, energy, and gas-exchange was obtained. This information was mostly obtained by combined direct and indirect calorimeters in highly specialized laboratories, measuring both heat and gas exchange as well as performing chemical analysis of food and its substrates.
A solid link between direct and indirect calorimetry was created, still fully valid today, and together with advances in electronics, analysers, and computer sciences this enabled the proliferation of indirect calorimetry in favour of direct calorimetry. Effectively, it appears that the complexity and cost of indirect- and direct calorimetry have switched places. This proliferation of indirect calorimetry was further driven by the appearance of commercial small mobile indirect calorimeters for bed-side and sports-lab applications.
In 1985 Paul Webb predicted that human direct calorimeters will grow in numbers, an expectation that has been superseded by a reality where small indirect calorimeters can now be found in nearly every hospital or food/sports-related institution world-wide. Effectively there are thousands of small, and 30-50 large, indirect calorimeters in operation today; only a single larger direct calorimeter remains. This broad proliferation of what must be considered a method sensitive to methodological and technical errors is problematic; gone are most of the specialized laboratories of the past, replaced by black box technology and/or operated by non-specialized personnel.
The relevance of the Human Energy Expenditure can be understood when viewing it as the counterpart to energy intake; the absorbed food. For a stable weight the expenditure must be matched by the intake, if these two are not in balance we either loose or gain weight.

> "Food may be defined as material which, when taken into the body, serves to either form tissue or yield energy, or both" (Wilbur Olin Atwater).

The energy balance of man is one of great importance to the world population; every single person needs sufficient and healthy food. Obviously, this is not the case, whole populations are starving while others become morbidly obese. A problem of the distant past and of even greater interest in future; how do we feed a 10+ billion world population? How to solve the myriad of health problems traceable to over- and underfeeding? Or sleep, activity and environment? Or even, how do we feed astronauts during their travels to Mars? The scope of questions is growing and seemingly endless, and it can be

envisioned that multi-disciplinary research is not only required but will grow and result in additional research topics.
The above may determine the current status of measuring Human Energy Expenditure as a wide-spread and important tool that nowadays may, sadly, lack local support and specialized know-how. Effectively, results may be contradictory and even detrimental to the solid foundation of information of the past. Moreover, application for the individual clinical assessment can be problematic.

> "Many research workers in medicine and other fields of biology have embarked on calorimetry in the mistaken belief that measurement of oxygen consumption and hence energy expenditure is a very straightforward process. It is almost certain that results and conclusions which have been reported from some calorimetric systems are incorrect." (McLean and Tobin)

The value for research in Maastricht

With roots in classic calorimetry, progressing from chemical analysis of the past to electronic analysis of today, developments in human calorimetry at Maastricht University proved successful. Its value for research can only be recognized from the thousands of subjects that have been measured, the hundreds of papers that have been published, and the numeous industry contracts on topics of food, equipment and medicine that have been fulfilled.
Value also resulted from the actual calorimeter systems as developed in Maastricht, starting in 1983 with improvements to commercial bed-side calorimeters (under non-disclosure at the time), which financed PhD studies that were executed with the prototypes build in Maastricht. And resulting in today’s commercial availability of Omnical branded calorimeters on the global market.

Academic help versus commercial turn key systems

From 1995 onward help to other research groups around the world was provided from Maastricht, a common academic practice, resulting in more or less successful whole room calorimeters around the world. In Madison (USA) dr. Keesey's lab built a true copy of the Maastricht system that was successful from the start. In Capetown (ZA) there was a failed calorimeter that gained functional status by modifying key parts to resemble the Maastricht system. In Japan (JP) there are 8 calorimeters similar to the Maastricht calorimeters yet with a different gas analysis system. In Wollongong (AU) a copy was built but never completed to full copy status or functionality.
Based on the partially negative experiences gained, the next projects were full turn-key systems delivered by the company “Maastricht Instruments” to medical schools in War-

wick (UK) and Singapore (SG). Interest in these turn-key solutions is strong, yet the sizeable installation and cost in the end may allow 1 in 10 research groups to finalize funding.
Aside from these high-performance whole room calorimeters the bed-side and sports type Omnical as applied in the MRUM (Metabolic Research Unit Maastricht) has now become commercially available, and first reactions from the field of calorimetry indicate interest in these small calorimeters as well.
The Omnical calorimeters are different from the competition regarding the chosen components and applied methods; high-end components are intended to provide a continuous 24/7 quality of gas analysis, lowering drift over time and increasing quality over the duration of studies. Importantly, the devices can be checked on-site. The specifications are a direct result of the researchers needs as learned in 35 years of calorimetry in Maastricht, and delivering turn-key equipment eliminates the chances of failure that was experienced in part when groups where "*building one up from components*" with academic help from others. Caveat emptor: successfully building one remains the best course training, it is also the most expensive solution and especially if unsuccessful.

> "Whether buying a complete system or building one up from components, it is necessary to have a full understanding of the basic principles and of the many sources of error that must be guarded against." (J. A. McLean & G. Tobin)

A counterweight to ignorance

It has been stated that human indirect calorimeters have proliferated as "black boxes" and results may certainly suffer from absence of specialized know-how.
In some instances, literature, or papers submitted for review, dismiss biological reproducibility or have no biological data at all, which may be considered pure ignorance beyond a lack of know-how. It is a commercial routine to advise checking a calorimeter in one mode, and then let it be applied in a different mode; this certainly does not validate the calorimeter for the intended use.
In contrast, the calorimetric systems proposed in this thesis, now branded "Omnical", may be validated on-site, frequently, and in the identical mode as applied with subjects. This approach revealed near-identical variability on the technical and on the biological aspects (this thesis), and both technical and biological validity may be deemed a requirement for successful operation of human calorimeters.
Importantly, in a recent comparative study (just submitted by colleagues in the US) the Maastricht Omnical proved most reproducible and reliable of all calorimeters tested, which typically is of value for the individual assessment of a patient.
Please note that application of the presented calorimeters should not be considered a haughty claim to infallible measurements, instead it should be considered an eye-opener as to how much can and will go wrong; in this regard ignorance is not bliss!

> A common mistake that people make when trying to design something completely foolproof is to underestimate the ingenuity of complete fools.
> (Douglas Adams)

The emerging reality of calorimetry

As human calorimetry evolves and proliferates the need for locally validated equipment will rise above the clouds of more or less useful validation studies. Researcher will require proof of suitability of their locally applied device, not simply rely on a paper that tested "a" unit at some point in time. No device can simply be deemed a gold-standard apparatus without periodically checking if it still operates correctly, and if anyone learned this lesson; we did and we still do.
Moreover, longitudinal application of calorimeters is an under-rated yet important aspect; a 6 month check with repairs may confound results of the before- and after repairs intervals; this will not do, results must be constant in quality over the duration of a study.
Recent co-operation between research groups shows the growing awareness about these aspects; it may be the dawn of truly validated research, even for the users of "black box" technology.
The calorimetry systems as applied in Maastricht are expected to take part in this emerging reality of continuous and longitudinal productivity of calorimetric measures. With 16 calorimeters up and running on a 24/7 basis the demands upon quality control and validation testing are higher than ever before, and even after 35 years of operation and innovations it is possible to find unexpected errors. The technical and operational lessons learned will continue to lead to solutions that find their way into day-to-day operations and guidelines.
Problematic in this process is the multi-disciplinary combination of technical and biological aspects; technical papers that are legible to biologist may be too low on biological content to be acceptable for the biological papers. Their already educated editors and reviewers may simply consider it required common knowledge, even if sadly this knowledge is no longer that common. This conundrum exists, and a solution to this problem may be to expand the availability of calorimeters that indeed can be validated on site, by the local researcher, and also to provide training together with the equipment. This is one reason for providing the calorimeters as applied in Maastricht to colleagues; proof of validity by being reproducible at other sites.
Innovative in this regard is the adherence to classic and proven methodology, augmented with the precision and accuracy of modern technology; it may cost more and take more space, but it will be reliable and validated.
The chances for this type of equipment and methodology on the market are good, although starting with small numbers the production can be easily scaled up as demand grows. With the advent of comparative papers and the option to test these devices

before final purchase researchers and clinics may recognize the increased value of reliable results and long lifespan. A first problem will be the many papers on validity of other commercial equipment, yet they do not incorporate aspects of performance over time and cost of ownership regarding questionable results. This is the new frontier, and calorimeters, especially for "black box" application, must perform at a constant quality and prevent operator errors. They should simply work but also provide continuous proof of validity.

> "Simplicity is the ultimate sophistication. It takes a lot of hard work to make something simple, to truly understand the underlying challenges and come up with elegant solutions." (Steve Jobs)

In conclusion

There is a large demand for simple yet accurate human calorimeters; thousands of units exist worldwide. There is also a demand for highly precise whole room calorimeters, this requires a level of infrastructure and funding to a degree that just a few sites will be able to realize in the near future; maybe more when time goes by and turn-key systems prove their value. Possibly a demand for a few direct calorimeters will return; they provide information on a different aspect on human energy expenditure.

> "The measurement of respiratory gas exchange, or of metabolic rate as an alternative term, is something quite different from the measurement of heat from the body. It is an assessment of how much fuel has been oxidized, and with what proportions of fat to carbohydrate, if the oxidation of protein is known." (Paul Webb)

The results of studies performed with the current equipment in place will show its success or expectedly lack thereof, opening opportunities for selling, hiring out and building a reliable and simple to operate class of calorimeters. The latter is the class of equipment targeted by developments in Maastricht; we too require these simple yet accurate human calorimeters and have a need to validate them regularly.

After co-developing commercial units, that deviated from their original design over time and did no longer meet our requirements, the only option was to go back to our original prototypes and build upon those. This is now a requirement, and this time around we hope to keep calorimeters originating from Maastricht in line with the demands and possibilities of our metabolic research unit.

It will be interesting to see how commercial and research needs may come together and provide worthwhile solutions to a changing world of calorimetry.

> "You can't look at the competition and say you're going to do it better. You have to look at the competition and say you're going to do it differently." (Steve Jobs)