Bio-Images Research Ltd.

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Bio-Images Research Ltd., a leader and at the forefront of innovation in gamma scintigraphy, undertakes early-phase clinical studies to streamline drug development processes and assists decision-making. Founded in 2000 by Professor Howard Stevens and Professor Clive Wilson, Bio-Images Research Ltd. (Glasgow, U.K.) is a spin-out company from the University of Strathclyde. The company, based within Glasgow Royal Infirmary, undertakes early-phase clinical studies in volunteers and patient groups, specialising in gamma scintigraphy.

Professor Wilson, together with colleagues at Queen's Medical Centre, Nottingham, U.K., was one of the pioneers in the application of scintigraphic imaging techniques in drug research. Gamma scintigraphy allows non-invasive visualisation of drug formulations and body systems. A gamma emitting radiopharmaceutical, typically ^{99m}Tc or ^{111}In, is incorporated into the formulation before administration to the volunteer or patient, allowing images to be acquired at precise intervals over a period of time. The emitted radiation is captured by the gamma camera to produce scintigraphic images.

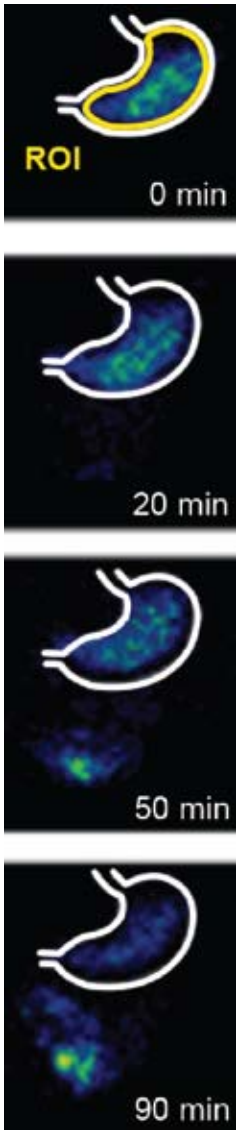

Figure 1. *Gastric emptying.*

Analysis of these images provides qualitative and quantitative information on formulation behaviour *in vivo*. By drawing a region of interest (ROI), for example around the stomach in an oral drug delivery study (Figure 1), it is possible to transform scintigraphic images into radioactive counts, which can be used to determine *in vivo* kinetic behaviour of a formulation, such as the creation of gastric emptying curves (Figure 2) (1). Dual isotope studies can also be performed that would allow, for example, evaluation of a tablet formulation containing both immediate release and controlled release technologies.

Applications of this technology in the field of oral drug delivery include the evaluation of buccal drug delivery systems, oesophageal transit studies, analysis of gastroretentive dosage forms, gastric emptying studies, gastrointestinal transit, food effects, intra- and inter-subject variability, and site of delivery, such as the investigation of formulations designed to target the colon.

A recent study by Ghimire et al. (2) illustrates the use of gamma scintigraphy to determine the erosion behaviour of a controlled release matrix tablet. During *in vitro* studies, the addition of ^{99m}Tc-labelled charcoal to a wax matrix tablet allowed erosion to be monitored using the gamma camera (Figure 3). Following a clinical study in volunteers, *in vivo* erosion behaviour was determined using the scintigraphic images acquired (Figure 4). This allowed an *in vitro–in vivo* comparison to be made for the controlled release tablet (Figure 5).

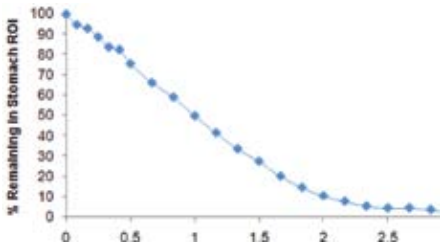

Figure 2. *Gastric emptying curve.*

It is particularly informative when a scintigraphic study is coupled with blood

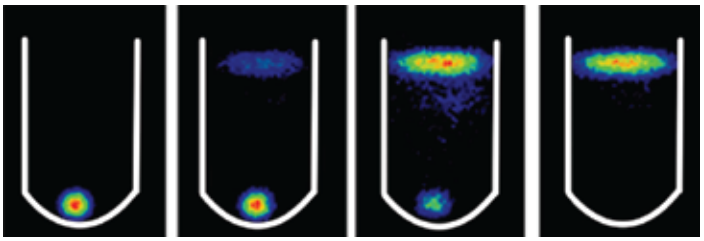

Figure 3. In vitro *erosion.*

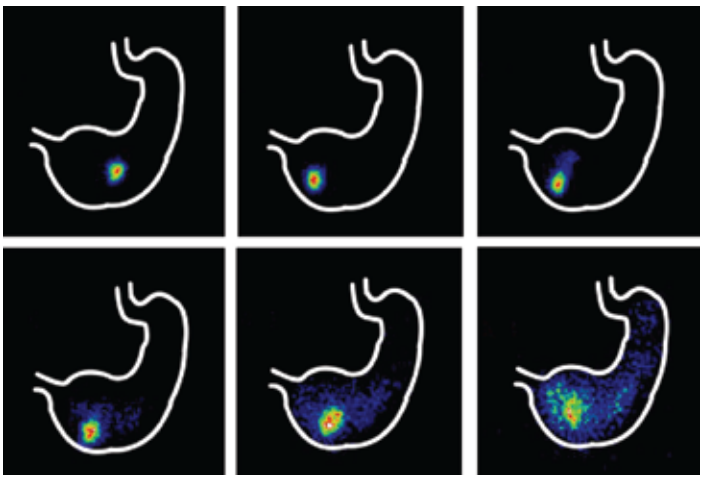

Figure 4. *Typical images* in vivo.

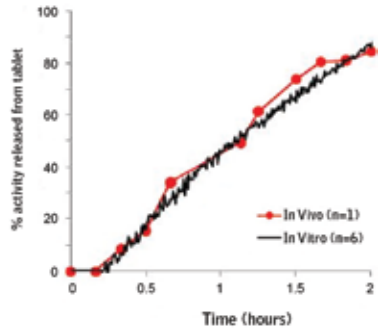

Figure 5. In vitro-in vivo *comparison*.

sampling, permitting drug pharmacokinetic parameters to be determined. The PK data can be interpreted more fully when accompanied by evidence of where the dosage form was located at a given moment and whether it underwent any physical change. Figure 6 shows a pharmacokinetic profile for three time-delayed capsule formulations containing the model drug theophylline (3). Accurate scintigraphic information, both alone and in combination with pharmacokinetics, will assist in drug development decision-making, including the development of new formulations, re-formulation of existing products, and marketing.

In addition to applications for oral drug delivery systems, gamma scintigraphy is also routinely used to investigate nasal, ophthalmic, and pulmonary formulations. Studies can be conducted, for example, to assess the residence of bioadhesive nasal or ophthalmic formulations, determine the clearance of these preparations (4), assess absorption enhancers, quantify lung deposition, and correlate inhalation performance with PK data. Bio-Images has extensive experience in designing suitable labelling techniques for new formulations and delivery systems.

Bio-Images recently acquired the breakthrough technology, the imaGIT® capsule. ImaGIT®, licensed from Casper Associates, is an ingestible, radio-controlled device used to evaluate regional drug absorption.

Employing Bio-Images' leading non-invasive gamma scintigraphic imaging techniques, imaGIT® is tracked through the digestive tract following oral administration, and on arrival at the desired target site, release of the contained drug is triggered by an external radio signal. Blood sampling following drug release allows assessment of bioavailability, the results of which assist pharmaceutical companies to rationalise their formulation development strategies. The imaGIT® capsule reduces development time and costs through identification of drug absorption sites, rationalises development of modified release preparations, and permits a targeted dosage form to be developed for regions of maximum absorption.

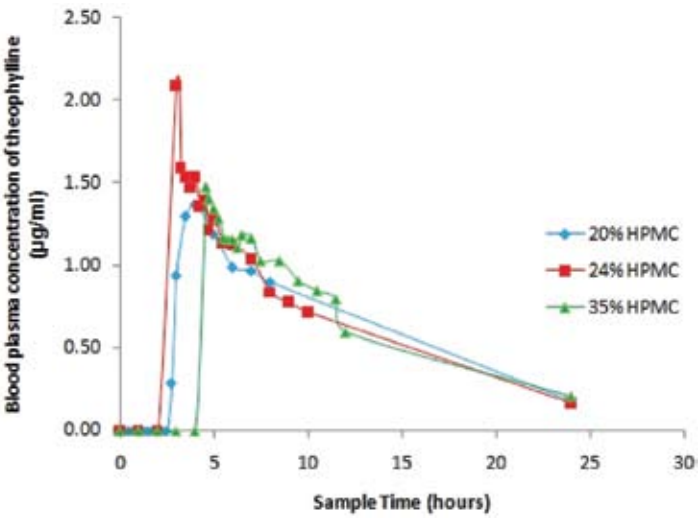

Figure 6. *Pharmacokinetic profile for three time-delayed formulations in subject 001.*

Preclinical studies are also conducted in a purpose-designed facility equipped with a gamma camera, enabling a full range of scintigraphic studies to be undertaken. Preclinical gamma scintigraphy offers the possibility of conducting such studies at an earlier stage than might be possible in humans, and pharmacokinetic studies can also be performed (5).

Bio-Images has secured numerous blue-chip customers in Europe, the United States, and Japan and has delivered six steady years of top-line growth and profitability. The recent announcement of its strategic partnerships in the United States and Japan will enable Bio-Images to expand its expertise and customer base. These alliances will allow new customers access to the range of Bio-Images' clinical services, including

- A hospital base that allows access to defined patient groups and specialist medical support
- Connections with world-renowned experts
- University links that provide access to new technologies
- A proven track record for innovative radiolabelling techniques Experienced staff dedicated to quality of service
- Competitive costs

The company have also completed validation of a fully compliant cGMP manufacturing facility at their clinical research unit in Glasgow. The manufacturing authorisation is a major event in the company's evolution, bringing manufacturing operations in-house and providing streamlined service to clients.

References

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