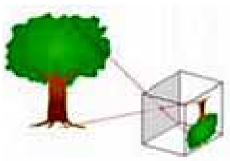
MEET MOLLYQ™

A new tool for molecular imaging of live animals for drug discovery and development based on single-photon microscopy.

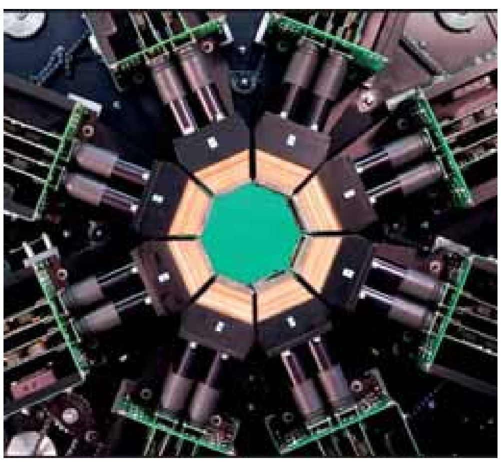
The pinhole camera To appreciate the advances made by the MollyQ™ it is useful to understand the many inherent limitations of current SPECT (single-photon emission computed tomography) technology that is based on the *pinhole camera*. This is not old technology, this is ancient history.[1] Forming an upside down image by using a pinhole was described in Chinese texts from the fifth century BC. By the tenth century it was realized that the smaller the pinhole the clearer the picture and the first camera *obscura* was set up.[2] Such cameras were later adapted by Louis Daguerre and William Fox Talbot for creating the first photographs.



In the last century, kids made pinhole cameras from light-tight shoe boxes with a pinhole at one end and a piece of photographic film or paper taped to the inside of the other end. The intrinsically low sensitivity of the pinhole camera makes it ideal for taking pictures of solar eclipses.

The pinhole gamma camera In the middle of the last century the pinhole camera was applied to imaging distributions of radioactivity within bodily tissues. The medical gamma camera replaced the film, and a lead container and pinhole replaced the cardboard shoebox. Like the optical pinhole camera, it is very insensitive. All the gamma rays from the radioactive object that do not make it through the lead pinhole are lost. Attempts to lessen exposure time by making the pinhole larger is paid for by making the image even fuzzier.

The no more compromises, always optimum, MollyQ The MollyQ™ was invented to overcome the many intrinsic problems of the pinhole gamma camera — *it does not use either pinholes or gamma cameras*.



Instead, the technology is similar to the scanning optical microscope used to create three-dimensional (3D) images of tissue samples. This device uses a wide-aperture lens to produce a tiny focal point which is mechanically scanned to gather optical data over planes at successive depths. This data is then used to reconstruct a 3D image of the sample.

This is just the way that the MollyQ™ works. A wide aperture collimator replaces the wide aperture optical lens and the "planes" become uniformly-spaced "slices" along the axis of the object. An inside view of the MollyQ-50™ is shown in the picture.

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[1] Aristotle and Euclid

[2] Abu Ali Al-Hasan Ibn al-Haitham, an Iraqi Muslim mathematician, astronomer and physicist, in his Book of Optics (c. 1000). The camera *obscura's (Latin for 'dark chamber')* potential as a drawing aid may have been familiar to artists by as early as the 15th century; Leonardo da Vinci described camera *obscura* in Codex Atlanticus.

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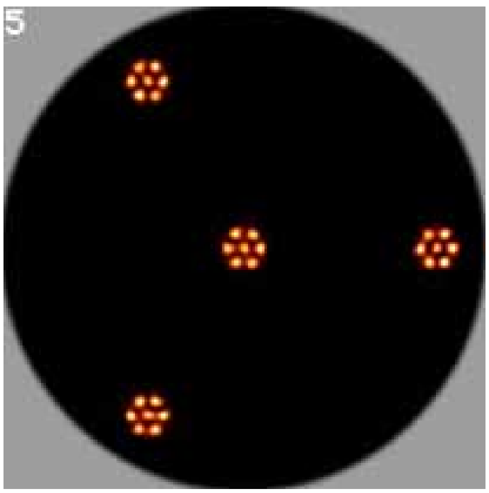
In order to maximize sensitivity, the MollyQ uses *eight* wide-aperture (67ºx45º) collimators. Each has 10,042 long-bore converging conical-holes producing a tiny focal point. The entrance holes of the collimators are only 343 microns in diameter and the slice-to-slice spacing is only 400 microns. A patent has been applied for.[3]

***In vivo* autoradiography** In use, the MollyQ is like autoradiography — assembling a 3D image of the radioactivity distribution in an animal from many slices. But, unlike autoradiography, it leaves the animal alive for ongoing longitudinal studies. A wide variety of labeled biological materials used in autoradiography are available for use with the MollyQ.

MollyQ's unmatched performance is fixed by geometry: Full sensitivity and resolution are constant over its full field-of-view! In all other "micro" SPECT animal imagers, one must trade between sensitivity, resolution and field of view. They cannot achieve their highest resolutions and sensitivities *simultaneously* and the best value of either parameter is only obtained by reducing the field-of-view.



An image you won't see anywhere else We devised a simple phantom to illustrate what the MollyQ-50™ can do that is impossible for pinhole cameras — or any other molecular imager. It contains 28 small sources grouped into four clusters (7 sources per cluster). Each source is a cylinder 2 millimeters in length and 800 µm in diameter and each cylinder contains only 1 µCi of activity (28 µCi total for all).[4] One cluster is at the center of the field of view and the other three are at a radius of 20 mm — locating them near the edge of the 50-millimeter field of view of the MollyQ-50™.

This image is the center slice of a reconstructed 10-minute simulated scan of this phantom that includes typical system background count rate and Poisson statistics.

Both very high, uniform spatial resolution over the entire 50 mm field of view and unexcelled sensitivity are simultaneously demonstrated

MollyQ is very friendly Like other user-friendly laboratory instruments, the small MollyQ sits on a bench top and is easily operated by a laboratory technician. It requires little power, floor space, maintenance, minimal QC procedures and is inexpensive. It is ready to perform when you are.

Our users like it Our University of Glasgow users published an abstract saying that, "*The instrument has the capacity for high performance pre-clinical drug discovery studies*," and our University of Massachusetts users have claimed that, "*This technology allows one to assess brain penetrance, pharmacokinetics, and dose occupancy of new CNS drugs.*"

[3] There are four models; MollyQ-30 (mice), MollyQ-50 (mice and rats), MollyQ-50m (marmoset monkeys), and MollyQ -200 (all large primates) where the number designates the field-of-view. The volume resolved depends on the FOV and is approximately 27 nL, 125 nL, and 15 µL respectively.

[4] Similar results can be obtained with 1 mm diameter tubes filled with only 250 nCi each (7 µCi total).

MOLECULAR IMAGING MODALITY COMPARISON			
	Positron Scanner	**Rotating Pinhole Gamma Camera**	**Scanning Focal-Point Microscope**
Instrumentation	Elaborate, requiring many detectors and very fast electronics	Old technology using pinholes with gamma cameras invented in 1957	Unique, uses highly focused collimators and minimal parts for artifact-free images
Size	Large, requires room	Large, requires room	Small, sits on table.
Cost	~$1,400,000 not including cyclotron	~$700,000	~$240,000
Emission of Radioactive Tag	511 keV Annihilation Photons	~140 keV Gamma Rays	~30 KeV X-Rays
Half Life	Minutes	Hours	Hours to Months
Source of Radioactivity	Near-by Cyclotron	Vender	Vender
Tagging Chemistry	Easy, but requires very fast (expensive) hot lab processing.	Complicated, but more time is available.	Many long half-life molecules can be purchased already tagged.
Volume Resolution (nanoliter)	Limited to 7000 nL by position travel	Depends on pinhole and FOV, ~3500 nL for rats	125 nL, constant over full 50 mm FOV.
Sensitivity	Intrinsically high, no collimation to absorb radiation	Very low, gamma rays must get through pinhole(s)	High, eight very large solid angle (f/0.9) collimators
Radioactivity required	Large because of short life-time	Large because of low sensitivity	Extremely low, 100 nCi in target can be imaged
Ease of Use	Requires large scientific staff to operate cyclotron, hot lab, and scanner	Requires physicists to keep gamma cameras running properly	Any laboratory technician can operate scanner
Coregistered Physical Imaging	CT	CT	MRI
Acronym	PET	SPECT	MollyQ™

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