Comparative Benchmark Dose Modeling as a Tool to Make the First Estimate of Safe Human Exposure Levels to Lunar Dust

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Background: Brief exposures of Apollo astronauts to lunar dust occasionally elicited upper respiratory irritation; however, no limits were ever set for prolonged exposure to lunar dust. The United States and other space faring nations intend to return to the moon for extensive exploration within a few decades. In the meantime, habitats for that exploration, whether mobile or fixed, must be designed to limit human exposure to lunar dust to safe levels (Fig. 1).

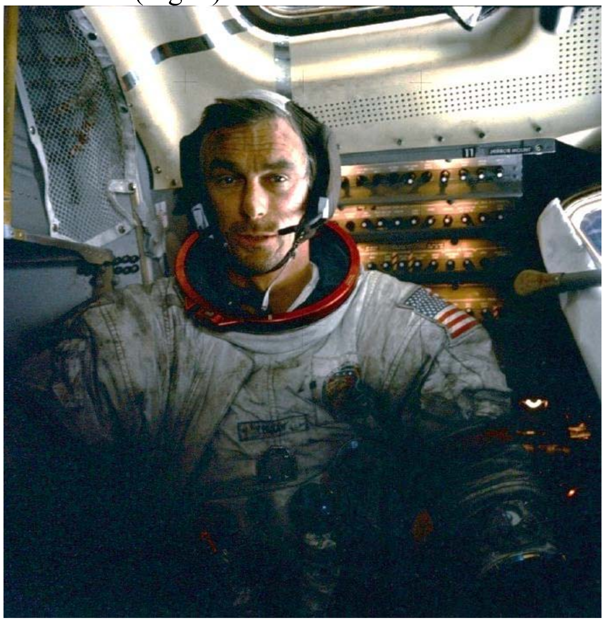

Figure 1. Astronaut Gene Cernan wearing suit covered with lunar dust.

We have used a new technique we call Comparative Benchmark Dose Modeling (CBMDM) to estimate safe exposure limits for lunar dust collected during the Apollo 14 mission. The US Environmental Agency provides software to perform benchmark dose (BMD) modeling. The goal of that modeling is to find a best fit to the dose-response profile for specific toxicological endpoints (Figure 2).

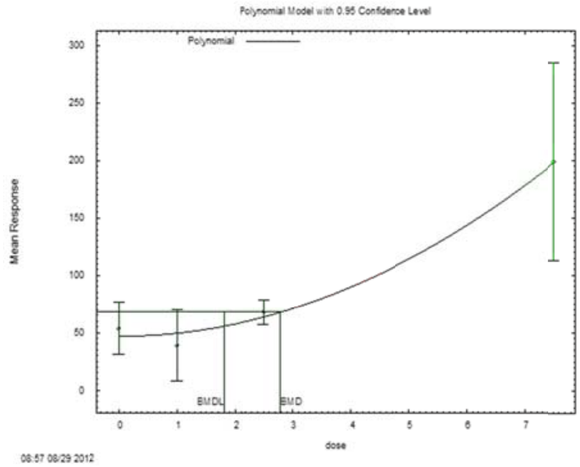

Figure 2. BMD curve that produced the best fit to data on monocyte chemotactic protein-1 a week after unground lunar dust was instilled into rat lungs. The BMD is approximately 2.8 mg.

Using the best fit profile, the user can select a level of risk of occurrence of an adverse event associated with the curve. We used the default measure of 1 standard deviation from the mean of the air-exposed control group.

Experimental Procedure: We instilled three respirable-sized (~2µ mass median diameter) lunar dusts (two ground and one unground) and two standard dusts of widely different toxicities (quartz and TiO_2) into the respiratory system of rats. Rats in groups of six were given 0, 1, 2.5 or 7.5 mg of the test dust in a saline-Survanta® vehicle, and biochemical and cellular biomarkers of toxicity in lung lavage fluid were assayed one week and one month after instillation.

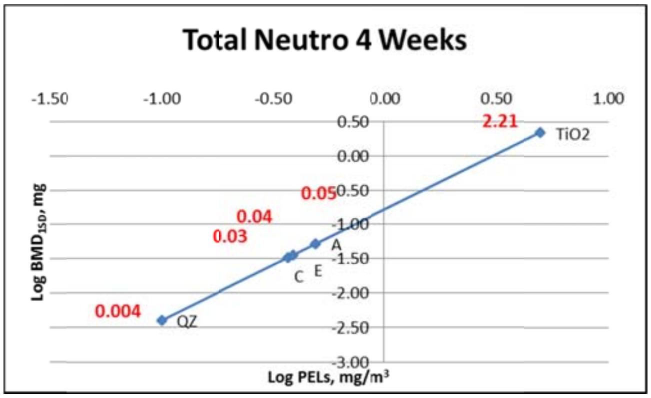

Figure 3. A log-log plot of the PELs vs. the BMDs for total neutrophil counts 4 w after dust instillation. A, C, and E represent the lunar dusts.

Benchmark Dose Modeling: A biomarker was deemed "sensitive" if the response to quartz (a highly toxic dust) was at least 10-fold higher than the response to TiO_2 (low toxicity dust). In addition, the benchmark fit to the data had to meet acceptability criteria for the fit to the data. By comparing the BMDs from the dose-response curves of sensitive biomarkers, we estimated safe exposure levels for astronauts (example in Figure 3). BMD comparisons were made to PELs that are known (Qz and TiO_2) and to be estimated (lunar dusts A, C, and E) on a log-log plot. The numbers shown in red are the log BMD values for neutrophil counts 4 w after dust instillation.

Lavage fluid biomarker	Jet-milled dust*	Unground (original) dust*	Ball-milled dust
Total white cells, 1 w	1.3	1.2	0.8
Total white cells, 4 w	1.4	0.6	1.1
Neutrophils, 1 w	0.5	0.9	0.5
Macrophages, 1 w	1.4	1.2	1.2
Macrophages, 4 w	1.7	0.6	2.3
LDH, 1 w	1.3	1.2	0.9
LDH, 4 w	2.0	0.7	1.0
Macrophage stimulation, 1 w	0.9	0.9	0.6
Macrophage stimulation, 4 w	1.2	0.7	0.6
Average Safe Exposure Estimates (mg/m^3)	1.3 ±0.4	0.9 ±0.3	1.0 ±0.5

Results: The first step in this process was to establish a line on a log-log plot of the known permissible exposure levels (PELs) against the biomarker response, and then locate the responses to the lunar dusts on this line according to the response of each to the biomarker (Figure 3). Five biomarkers produced acceptable data at one or both time points (1 week or 1 month after instillation). The results are shown in the Table. From the tabulated results we concluded that unground lunar dust and dust ground by two different methods were not toxicologically distinguishable. The safe exposure estimates were 1.3 ± 0.4 mg/m^3 (jet-milled dust), 1.0 ± 0.5 mg/m^3 (ball-milled dust), and 0.9 ± 0.3 mg/m^3 (unground, natural dust) as shown in the table.

Discussion: The CBMDM approach has a number of advantages over conventional ways of estimating safe human exposure levels. The conventional way is to expose a test species to the material in question from this determine a no-observed-adverse-effect-level (NOAEL). This level is taken as the point of departure (POD), to which large and somewhat arbitrary uncertainty factors are applied. These factors might include ones for interspecies differences, intraspecices differences, exposure time differences, etc.).

Our approach anchors the estimates for lunar dusts to the PELs of 2 dusts that have well-established PELs based on extensive data, both in test species and in humans. There is a single common control (vehicle exposed) for all 5 dusts, which makes comparisons more precise. The BMD analysis also uses all the data from the dose response profiles instead of just a single-point NOAEL. The profiles were generated using no more than 0.5g of lunar dust. Finally, multiple comparisons using a variety of toxicological endpoints, both biochemical and cellular can be used in forming the final estimates of safe human exposure levels.

The safe exposure estimates should be applied just like PELs are applied to earth based workers. Astronauts' exposures will be very similar to those workers. Depending on suit design, after each extravehicular activity (EVA) dust will enter the habitat and be scrubbed from the air over several hours. The plans are that EVAs will be conducted only during the work week and on weekends the astronauts will remain inside the habitat. This is parallel to industrial workers' exposures and is the basis assumed for the setting of PELs.

Conclusion: We estimate that 0.5 to 1 mg/m^3 of lunar dust is safe for periodic human exposures during long stays in habitats on the lunar surface. This is not currently an official NASA standard.

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