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# *In vivo* Performance of Nasal Spray Pumps in Human Volunteers By SPECT-CT Imaging

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A potential barrier to the widespread use of nasal spray devices for drug delivery has been the variability in dosing because of partial metering, as the patient does not press consistently enough on the actuator of the pump. This could be a serious limitation for the delivery of potent medications. Recently new generation nasal pumps have been developed by Valois which spray only on the full actuation of the pump, and hence ensure accuracy of dosing in intranasal delivery of drugs. The present study aimed to compare the *in vivo* nasal deposition pattern of two nasal spray pumps- a conventional pump (VP3®) and a new generation pump (EQUADEL®), both developed by Valois S.A.S, France, in human volunteers by SPECT-CT imaging technique.

## MATERIALS AND METHODS

Nasal spray pumps, VP3® and EQUADEL®, were fitted to 5 ml glass containers containing 1 ml of 0.5% methylcellulose in saline and $^{99m}$Tc DTPA (10-15 mCi). Viscosity was determined by rotational viscometer (Brookfield Viscometer, Model: LVT) and droplet size distribution by laser diffraction apparatus (Mastersizer X, MALVERN), Spray pattern by automatic actuating machine (Machine-NSX from Image Therm Engineering)[1]. For i*n vivo* studies, protocol was approved by Institutional Ethics Committee. Ten healthy male volunteers (20-30 y), screened by ENT surgeon were selected, and informed consent was obtained in writing from each volunteer. Tests were performed on three assembled units each of VP3 and EQUADEL in triplicate. CT scans (GE discovery ST) of all volunteers were recorded. For dosing, volunteers inhaled the spray in a sitting position, and SPECT images were recorded for 10 min, with volunteers in supine position. To calculate deposition area static image was analyzed; SPECT image was superimposed with CT scan, and nasal deposition was quantified in terms of upper to lower (U:L) and inner to outer (I:O) ratios[2] (fig. 1).

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## RESULTS AND DISCUSSION

Rheograms of 0.25% MC sample (pH 5-6) have shown pseudo-plastic behavior. Droplet size distribution in case of VP3 was slightly larger than EQUADEL (Table 1). Spray pattern analysis showed more variability in case of VP3, although the mean values for both pumps were similar (Table 2). In the *in vivo* study, the SPECT images were superimposed with CT scans and deposition patterns of the two pumps were compared[3]. The data was analyzed by using Graphpad Prism 4 software. Analysis of the superimposed images revealed that for the I:O

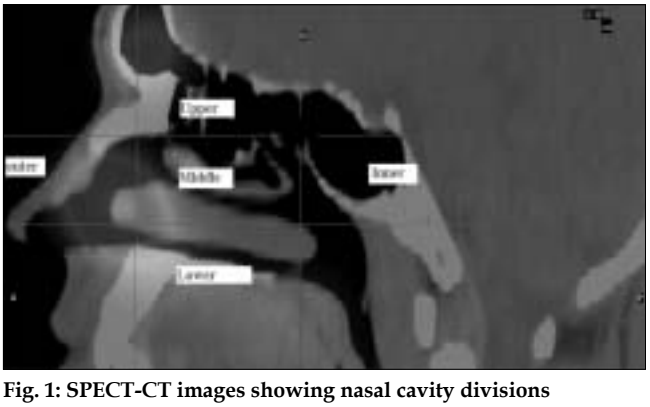

**Fig. 1: SPECT-CT images showing nasal cavity divisions**

**TABLE 1: DROPLET SIZE DISTRIBUTION OF TWO PUMPS**

| Droplet size distribution D (V, 0.5) µm | | |
|---|---|---|
| | Mean | RSD |
| EQUADEL | 49 | 6% |
| VP3 | 60 | 11% |

**TABLE 2: SPRAY PATTERN DATA OF TWO PUMPS**

| Spray pattern | Max. mm. | Min. mm |
|---|---|---|
| EQUADEL | 42 ± 3 | 35 ± 1 |
| VP3 | 42 ± 5 | 35 ± 4 |

**TABLE 3: REGIONAL DEPOSITION PATTERN AND DEPOSITION AREA OF DROPLETS ADMINISTERED BY VP3 AND EQUADEL PUMP**

| Volunteer | U:L | | I:O | | Deposition area (pixel) | |
|---|---|---|---|---|---|---|
| | VP3 | Equadel | VP3 | Equadel | VP3 | Equadel |
| 1 | 1.123±0.644 | 0.920±0.923 | 0.088±0.086 | 0.217±0.287 | 48.33±11.93 | 49.67±12.10 |
| 2 | 0.191±0.273 | 0.749±0.557 | 0.533±0.422 | 0.285±0.080 | 45.67±3.06 | 53.00±1.00 |
| 3 | 0.080±0.130 | 0.052±0.068 | 0.311±0.339 | 0.251±0.133 | 50.67±8.74 | 41.67±4.62 |
| 4 | 0.012±0.007 | 0.030±0.021 | 0.945±0.943 | 0.542±0.631 | 50.00±9.64 | 55.70±10.02 |
| 5 | 0.924±0.503 | 0.646±0.339 | 0.237±0.056 | 0.479±0.498 | 63.50±30.41 | 46.95±23.40 |
| 6 | 0.875±0.491 | 0.344±0.166 | 0.385±0.092 | 0.148±0.097 | 54.33±13.05 | 47.67±5.77 |
| 7 | 0.674±0.520 | 0.492±0.207 | 0.199±0.016 | 0.043±0.075 | 59.00±12.53 | 42.00±6.24 |
| 8 | 0.214±0.331 | 0.009±0.016 | 0.035±0.061 | 0.085±0.134 | 40.00±11.14 | 45.67±20.41 |
| 9 | 0.369±0.220 | 0.504±0.437 | 0.613±0.260 | 0.710±0.539 | 48.33±7.02 | 49.67±4.62 |
| 10 | 0.497±0.731 | 0.567±0.464 | 0.147±0.228 | 0.079±0.128 | 33.33±3.21 | 41.33±24.38 |
| Mean | 0.496±0.387 | 0.431±0.317 | 0.349±0.280 | 0.284±0.224 | 49.32±8.69 | 47.33±4.64 |

Nasal deposition was quantified in terms of radioactivity deposited in inner (I) vs. outer (O), and upper (U) vs. lower (L) regions of the nasal cavity (Data presented are mean±SD, n=3)

and U:L ratios the Equadel pump had less variable deposition when compared to the VP3 pump (Table 3). Some differences between deposition areas (pixel), which corresponds to total dose delivered, are evident; however, these results are not strong enough to differentiate two pumps.

In conclusion, *in vitro* evaluation tests of the two pumps have shown slight differences and the *in vivo* deposition study showed the Equadel pump to have less variability of deposition. The study reveals the potential of SPECT-CT imaging technique to evaluate spraying devices/formulations for nasal delivery.

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