Validation of Birch Pollen Distribution in an Allergen Challenge Theatre™

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Abstract

Rationale: Birch pollen is a common cause of allergic rhinitis but variability in the duration and intensity of the pollen season complicates the assessment of treatment effectiveness. Allergen challenge facilities expose sensitive subjects to stable allergen levels in a controlled environment, reduce variability in clinical symptoms and facilitate the evaluation of medication effectiveness.

Methods: We performed a technical evaluation of the capabilities of the Red Maple Trials Allergen Challenge Theatre™ (ACT) - an allergen challenge facility to generate a consistent, stable birch pollen concentration. The ACT is a 4-zone facility holding up to 100 seats in a series of elevated rows. Birch pollen (Betula populifolia) was injected into the air supply and blown into the facility through a series of movable horizontal vanes located across the top of the front wall. Adhesion of pollen grains to the surfaces of the ACT was minimized by the use of antistatic materials. Birch pollen concentrations in the ACT were measured over time with two methods: impact samplers (IS) and laser particle counters (LPC) to measure the concentration in the ACT as well as to determine the correlation between these two methods. IS and LPC samplers were positioned 1.5 m above floor level. An independent LPC measured pollen concentrations at ceiling level near the supply duct and served to control the pollen generator. The relationship between IS and LPC pollen counts was determined from 15-minute measurements as pollen levels were increased in steps of 1000 from 1000 to 6000 grains/m³. Uniformity of pollen levels was determined from LPC readings in different parts of the room. Long-term stability was assessed by continuous LPC recordings at a constant pollen concentration. he supply duct and served to control the pollen generator.

Results: A very close linear relationship was achieved between the LPCs and the IS (controller, R² = 0.999; room LPCs, R² = 0.970). Pollen counts were within ±30% from side to side and ±60% from front to back. Birch pollen supply levels were constant at (3992 ±370) for 190 minutes.

Conclusions: The Red Maple Trials ACT demonstrated the capacity to achieve and maintain birch pollen levels of 4000 grains/m³ throughout the room consistent with those reported in the literature and associated with the ability to induce symptoms of appropriate intensity. Pollen counts measured by LPC and IS were tightly correlated.

Introduction

Birch and other trees of the genus Betula are common in North America and northern Europe and their pollen is one of the causes of allergic rhinitis symptoms in the spring. It is believed to be one of the most reactive of all tree pollen affecting approximately 20-25% of the population living in these northern latitudes. In Europe, the start of the pollen season varies from the end of March to late May depending on the location and temperatures. The season begins as the birch tree buds mature and release pollen grains into the air. The duration of the season is dependent on temperature and humidity and varies from 2 to 8 weeks (30 minutes). In consequence, multi-centre clinical trials to test treatments for birch pollen allergy require precise timing and large patient populations. In contrast, allergen challenge facilities expose subjects to a constant and stable allergen load in a temperature, humidity and airflow controlled environment, thereby reducing the variability in clinical symptoms and facilitate the evaluation of medication effectiveness. The purpose of this study was to validate the Red Maple Trials ACT (a 4-zone facility holding up to 100 seats in a series of elevated rows, Fig. 1a) for testing birch pollen to ensure that the facility generated a consistent, stable birch pollen concentration (Fig. 1b).

Birch pollen (Betula populifolia) was introduced into the air supply and blown into the ACT through a series of movable horizontal vanes located across the top of the front wall. Adhesion of pollen grains to the surfaces of the ACT was minimized by the use of antistatic materials. Birch pollen concentrations in the ACT were measured over time with two methods: impact samplers (IS) and laser particle counters (LPC) to measure the concentration in the ACT as well as to determine the correlation between these two methods. IS and LPC samplers were positioned 1.5 m above floor level. An independent LPC measured pollen concentrations at ceiling level near the supply duct and served to control the pollen generator. The relationship between IS and LPC pollen counts was determined from 15-minute measurements as pollen levels were increased in steps of 1000 from 1000 to 6000 grains/m³.

Results

Mature birch pollen becomes airborne following the release from the tree catkins. They appear spherical in appearance with three exodisc flanges. Under natural exposure conditions, individual whole grains have a mean diameter of roughly 20 μm (Fig. 2a and 2b).

LPC1 and Impact Sampler Correlation

As shown in Fig. 4a, there is a very good correlation between LPC1 which is controlling the pollen concentration in the room and the IS over the corresponding size ranges. We observed a similarly strong correlation between the other LPCs within the ACT and the corresponding IS (Fig. 4b). This is a typical figure that we would use in which the IS devices were used to align the LPCs during a 150 minute run.

LPC1 versus Impact Sampler Correlation

Fig. 3. IS and LPC counts increase proportionally as the pollen delivered to the ACT is increased.

Correlation between LPC and Impact Samplers

The IS readings were shown to increase as the target pollen concentrations were increased. The individual sampler readings were highly comparable and consistent to the LPC readings with the standard deviations low (Table 1) in the 190 minute test period.

Table 1. Target versus actual birch pollen concentrations. Impact Sampler values are derived from a 25 minute collection time from two 2nd Rotation (a and b) samplers.

Conclusion

Computational Fluid Dynamics (CFD) has been shown to be an invaluable tool to provide an extensive understanding of how to achieve accurate and consistent pollen concentrations throughout a large chamber. Our previously reported validation studies with grass and ragweed pollen confirmed the ability to achieve the desired pollen concentrations. The system has been shown to be stable and the pollen levels to be reproducible. Building upon this experience with CFD we continued to use this knowledge as a basis to direct the technical development and validation of the ACT for birch pollen.

Building on this experience we have now demonstrated our system has the ability to achieve and maintain birch pollen levels between 1000 and 6000 grains/m³. This range is consistent with what has been reported in the literature and associated with the ability to induce ocular and nasal symptoms of appropriate intensity. Pollen counts measured by LPC and IS were highly correlated with tight standard deviations.

The Red Maple Trials ACT is a high capacity, modular, state of the art facility capable of evaluating 100 participants at a time. This allows us to obtain accurate and reproducible results in a timely and cost-efficient manner, thereby providing the technical insight for sponsors conducting field exposure studies.

References

Bernstein, J.A., ed. Correlation between a pollen challenge chamber and a natural allergen exposure study design for eliciting ocular and nasal symptoms: Early evidence supporting a paradigm shift in drug investigation? Journal of Allergy and Clinical Immunology. 2012; 130: 126-129.


Fig. 4b. Correlation between chamber LPC and IS samplers.