Using Pixel-Based Visualizations to Detect Adverse Drug Events

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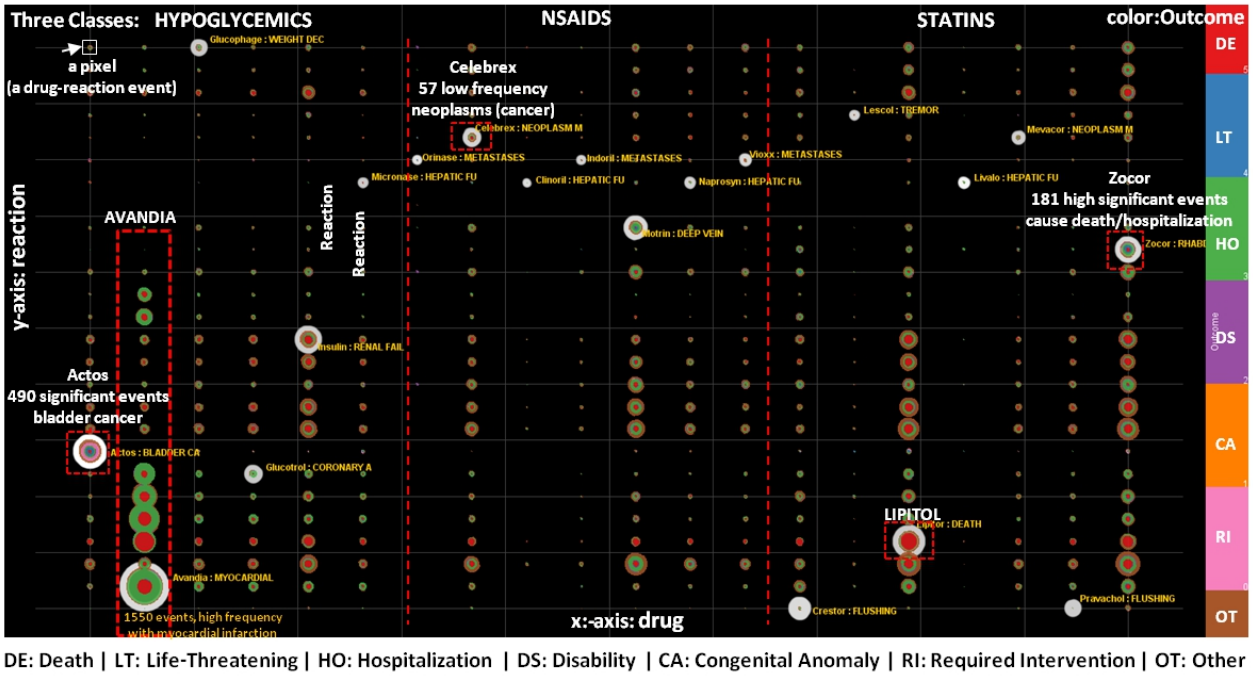

Figure 1: Visual Analytics of three classes of selected drugs and adverse events from the FDA Adverse Event Report System
Each coordinate location (pixel) represents a drug-reaction event in a non-overlapping scatter plot. The size of the circle represents the number of events that occurred for a drug. The size of the white rings encodes the significance of the event. From both the size of the circle and its brightness, physicians can quickly learn which events (drug-reactions) are most significant as illustrated by the red dashed rectangles.

Abstract

Adverse reactions to drugs are a major public healthcare issue. Currently, the Food and Drug Administration (FDA) publishes quarterly reports that typically contain in the order of 200,000 adverse incidents. In such a large number of incidents, low frequency events that may be highly clinically significant but are often undetected. In this *poster*, we introduce a pixel cell-based visualization technique with novel relevance ordering algorithm, significance statistics computation, and semantic zooming in an x-y plan. We are able to identify important adverse events, such as the known association of the drug Avandia with myocardial infarction; as well as low frequency events such as the association of Actos with bladder cancer.

1. Introduction

An Adverse Drug Event (ADE) is defined by the Institute of Medicine as "an injury event resulting from medical intervention related to a drug". Each year, about 98,000 drug-related deaths are reported in the USA.

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Even after a successful clinical trial in which a drug has been cleared for marketing to the medical community, unsuspected ADEs are occasionally detected. This is due to the fact that the trials are usually limited to short time periods and include a small number of patients. Also, the frequency of these adverse events may be so low that they are not found in the clinical trials. For example, in Figure 1, bladder cancer was not recognized as an adverse reaction to Actos until after Acots was prescribed to thousands of patients [1]. The current tools (e.g., Explorer and Web Scoreboard) are capable of detecting primarily high frequent events. Low frequency events are often overlooked. The problem addressed by our methodology is to develop visual analytics methods to detect low frequency, but significant adverse drug events.

2. Our Approach

A number of well-known statistical and machine learning techniques are available to analyze adverse drug events [2]. Most of them are able to cluster and classify the events according to their outcomes (e.g., Bayesian, Decision Tree, etc.). In contrast to the existing methods, we introduce a pixel cell-based visualization technique. First, we construct non-overlapping scatter plots for analyzing correlations between a large number of complex variables (e.g., drug and reaction). Next, we enhance statistical computations to quickly identify significant events including those with low frequency. Then, we employ interactive semantic

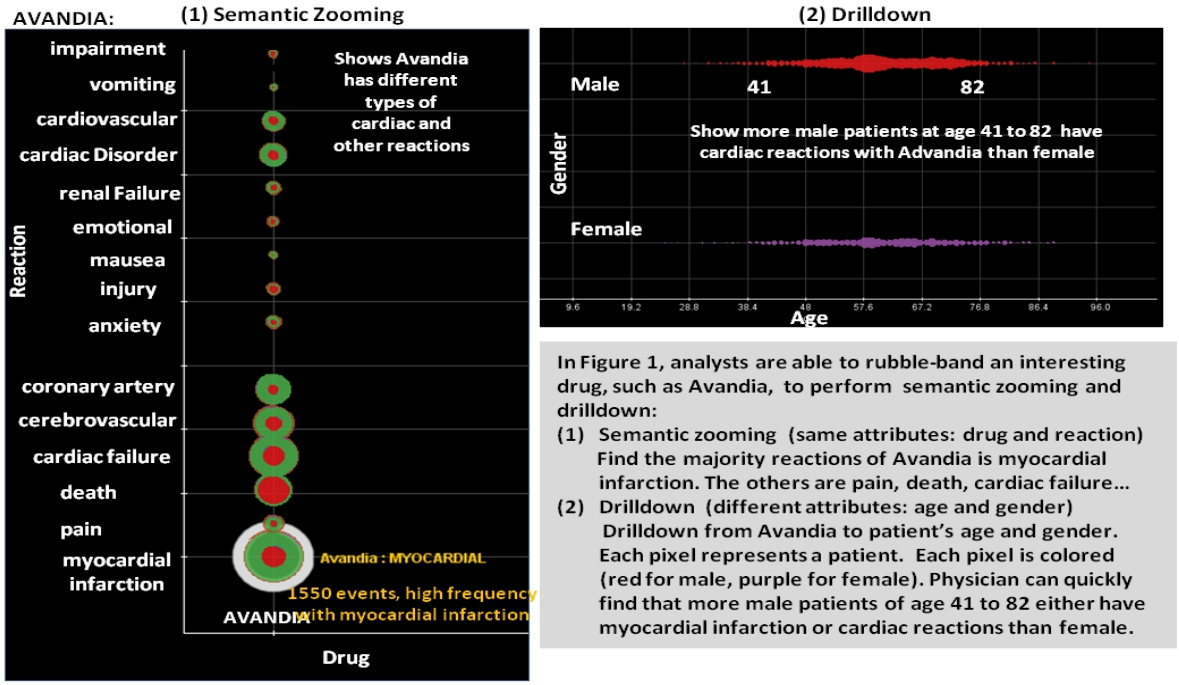

Figure 2: Semantic Zooming and Drilldown from AVANDIA in Figure 1

zooming and drilldown which help specialists to incorporate their expert knowledge into the process to detect adverse drug events. As illustrated in Figure 1, each pair of data point shows an event where the x coordinate represents a drug and y coordinate represents a reaction associated with that drug in a patient population. Color represents clinical outcome.

2.1 Event selection and ordering

First, we select a drug class (e.g., hypoglycemics) or a type of adverse event (e.g., myocardial infarction or type 2 diabetes) from the ADE user interface window. Next, we retrieve the relevant reactions [3] that are most frequently associated with the drug, and arrange the rows and columns according to drug class, and similarity. Finally, we display the resulting vectors on x, y axes in the pixel scatter plot shown in Figure 1 for expert analysis.

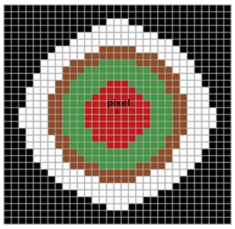

Figure 3: Non-overlapping circular pixel placement

2.2 Significance Computation

To determine the significance of events, we enhance Chi Square statistic method [1] based on the number of incidents occurring for each event. A reaction is a potential adverse drug event if it occurs more frequently in patients exposed to a particular drug than in patients not exposed to that drug. All significant events are highlighted with a white circle in the visualization (Figure 3).

2.3 Semantic Zooming

Domain experts can then interact with the display and select a group of interesting events for semantic zooming and drilldown as illustrated in Figure 3.

3. Evaluation

To demonstrate the effectiveness of our techniques, in Figure 1, we have applied them to detect adverse events from the FDA Adverse Event Reporting System. In the 4th quarter of 2011, the FDA reported 198,777 adverse events from 28,433 drugs that caused 9,295 reactions. We have discovered the following facts:

- Under the HYPOGLYCEMIC drug class, we found that Actos (pioglitazone), which is used to treat diabetes, has a significant association with bladder cancer. We see a significant number of outcomes in the Death (red) and Life-Threatening (blue) categories.
- Under the non-steroidal anti-inflammatory (NSAID) class, we found a low frequency but significant association between Celebrex and neoplasms (cancer).
- Under the STATIN drug class, we found drugs Lipitor and ZOCOR could cause death and hospitalization (red/green).

4. Conclusion

We have demonstrated that we are able to detect low frequency events from massive volumes of adverse drug events. Our next step is to continue our visual analytics work on drug interactions and actual drug usage over time.

References

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