Appendix A

Table 1: The visual signatures of the reviewed epithelial and sub-epithelial diseases.

Epithelial and sub-epithelial diseases	
The disease	**The visual signatures**
Amiodarone-induced keratopathy	– In the basal epithelial cells, white and adjacent inclusions appear that are small and have rounded-shape structures[24].
Advancing wave-like epitheliopathy	– Vertically stretched epithelial cells that have needle-shape and surrounded by a grey hazy halo with high intensity nuclei[25].
Epithelial basement membrane dystrophy	– Large area of light grey colour reflection can be seen with highly reflective nuclei that appear as white circles that have grey double-walled aureole[26]. – Many elliptic cysts with poorly defined borders[26]. – High reflective linear structure that has well-delineated anterior border[26].
Salzmann's nodular degeneration	– Highly reflective adjacent irregular and polygonal shaped basal epithelial cells appear with highly reflective nuclei that appear in each polygonal cell as a small grey dot[28]. – A nerve fibre appears as undulating sloping line with high intensity. Small bright dots appear on and beside the lower side of the nerve fibre[27, 28].
Gelatinous drop-like dystrophy	– Hyper-reflective and adjacent polygonal epithelial cells with irregular structure[29]. – Beneath the epithelium, amyloid materials appear as highly reflective accumulations spread in irregular ways[29].
Thygeson epithelial keratitis	– Highly reflective deposits with cotton-like appearance in the basal epithelial[30]. – Epithelial cells that look like cracked ground. These cells are disconnected and appear as high intensity curvy lines on a low intensity background. Small numbers of highly reflective spots also appear[30, 31].
Meesmann's dystrophy	– Well-delineated rounded shapes lesions surrounded by reflective points in the cytoplasm[26].

		– Multiple cyst-like changes which are very similar in size and distributed non-uniformly at the level of the basal epithelium with white colour while the normal cells have very dark grey colour with unclear borders[8].
Recurrent Erosion Syndrome		– A large area of high reflection with two bright white slanted lines over the epithelial mosaic[26].
Acanthamoeba keratitis	infective	– Highly reflective elliptic cysts within the corneal epithelium. These cysts could be single-walled structures that are very clear and varying in size, or could be double-walled structures with low intensity and thick border[1, 8, 16, 34, 35].
Bacterial keratitis		– Crowded hyper-reflective dendritic-like cells appear at stroma depths and the background can hardly be seen[8, 36]. – Thin, and short filamentous structures (Nocardia) that demonstrated right-angled branching surrounding by round to oval bright inflammatory cell[38].
Viral keratitis: herpes simplex virus		– Increase in cell size and hyperreflectivity while there is a decrease in cell density in the Superficial epithelium layer[39]. – Pseudoguttata possess a line of high reflection on the border of the elevated dark area, and intercellular gaps appear as small black dots at the vertices of endothelial cells[40].

Table 2: The visual signatures of the reviewed Bowman layer diseases.

Bowman layer diseases	
The disease	**The Visual signatures**
Reis-Bückler's dystrophy	– A high intensity elongated area with grey boundary that is interspersed with the basal epithelial cells[42]. – High reflective small granular materials replaces Bowman's layer. These granular materials group together as one big white area[43].
Thiel-Behnke dystrophy	– Deposits which appear hazy with different intensity values and cover a wide area of the basal epithelium. The edges of these hazy deposits have very low intensity undulating structure[8, 43]. – The Bowman's layer is completely hidden by reflective materials that appear as haze with different values of intensity and with some diffuse bright irregular spots[8, 43].

Table 3: The visual signatures of the reviewed stromal diseases.

Stromal diseases	
The disease	**The visual signatures**
Lattice dystrophy	– In the mid-stroma, small numbers of undulating and thin string-like structures of different lengths and high intensities interacting with the keratocytes which appear as hyper-reflective irregular shapes[44, 45]. – In the anterior and middle stroma, big bright tubular structure with well-defined edges interspersed with normal bright keratocytes. Keratocytes have irregular structures of different sizes[42].
Fleck dystrophy	– High intensity irregular large spots enclosed in a cyst-like structure throughout the stroma. A high intensity spherical area, relatively large, is connected with the cyst-like structure[8, 15, 47].
Granular dystrophy	– High reflective irregular deposits varying in size appeared in the anterior stroma with high intensity curved line[42]. – In the deep stroma, a large number of high intensity small deposits of punctiform structures are dispersed between high reflective rounded and oval shape keratocytes nuclei[42].
Schnyder crystalline corneal dystrophy (SCCD)	– High reflective and small elliptic material accumulated inside and around anterior keratocytes which have hypo-reflective irregular structures[50]. – In the anterior stroma, high intensity and well-delineated needle-shaped adjacent deposits largely bundled together[51]. – In the anterior stroma, some abnormal nerve branches can also be found. The nerve branches appear intersecting in the middle of the reflection area and have an irregularly curved shape[52].
Avellino corneal dystrophy	– At the level of the superficial and middle stroma, a high reflective cloud of granular materials appears that has irregular curvy borders with low intensity[48].
Macular corneal dystrophy	– High reflective accumulation of granules in the superficial stroma[43].

	– In mid-stroma, multiple hypo-reflective materials that have striae-like shapes appear. These linear shapes slope vertically and are thick[48].
Central Cloudy Dystrophy of François	– In the superficial stromal layer high reflective granules with irregular size groupings[54]. – Deep stroma appears as a hazy hyper-reflective background with many intersecting, low intensity, and thick lines[54].
Pre-Descemet's membrane corneal dystrophy	– Very small highly reflective dots interacting with normal keratocyte nuclei of anterior stroma[55]. – Posterior stroma shows hyper-reflective vesicles with irregular shapes containing bright granules[55].
Posterior amorphous corneal dystrophy	– Hyper-reflective sheet-like area which has spikes with medium intensity from the right side of it appearing in the posterior stroma[56].
Corneal amyloidosis	– Cotton candy-like reflection and fibrillar amyloid material that appears in the anterior stroma. This material has very uniform grey values[15, 57].
Fungal keratitis	– Fusarium solani reveals highly reflective hyphae of length (200-300) µm and of width (3-5) µm with branches at 90°angles in the anterior stroma and Round inflammatory cells are present [1, 58]. – Aspergillus hyphae have the same characteristics of Fusarium solani hyphae with branches at 45° angles[1, 58]. – Candida pseudiphilaments reveals high reflective elongated particles measure 10–40 µm in length and 5–10 µm located in the anterior stroma[1, 58].

Table 4: The visual signatures of the reviewed Descemet's membrane and Endothelial diseases.

Descemet's membrane and Endothelial diseases	
The disease	**The visual signatures**
Fuchs' endothelial dystrophy (Cornea guttata)	– Many roundish low intensity areas of different sizes with central light spots between the hyper-reflective endothelial cells which appear clearly[8, 15, 59, 60].
Iridocorneal endothelial syndrome (ICE syndrome)	– Endothelium appears as epithelium-like transformation with bright nuclei that appear as high intensity elliptic structures surrounded by unclear and irregular cell borders that have very low intensity[8, 61].
Posterior polymorphous corneal dystrophy (PPCD)	– Well-delineated roundish shape or elliptical endothelial lesions with low intensities near to black and appear in curvilinear pattern[8, 63].
Brown-McLean syndrome	– A highly reflective pigmentation intersperses endothelium cells which consists of an accumulation of bright round bodies with clear borders[64].

Appendix B

Table 5: Shape-based features extracted from the visual signatures of the reviewed corneal diseases.

Shape	Disease
Rounded (circle, ellipse, circular line)	**Epithelial and sub-epithelial:** • Amiodarone-induced keratopathy • Epithelial basement membrane dystrophy • Meesmann's dystrophy • Acanthamoeba infective keratitis • Viral keratitis: herpes simplex virus **Stromal:** • Fleck dystrophy **Descemet's membrane and Endothelial:** • Fuchs' endothelial dystrophy • Posterior polymorphous corneal dystrophy
Linear (stringy, elongated, needle-shape, tubular, striae-like, nerve, fibre)	**Epithelial and sub-epithelial:** • Advancing wave-like epitheliopathy • Epithelial basement membrane dystrophy • Salzmann's nodular degeneration • Recurrent Erosion Syndrome • Bacterial keratitis **Bowman layer:** • Reis-Bückler's dystrophy **Stromal:** • Lattice dystrophy • Schnyder crystalline corneal dystrophy • Macular corneal dystrophy • Central Cloudy Dystrophy of François • Fungal keratitis
Punctiform (granular)	**Bowman layer:** • Reis-Bückler's dystrophy **Stromal:** • Fleck dystrophy • Granular dystrophy • Avellino corneal dystrophy • Schnyder crystalline corneal dystrophy • Macular corneal dystrophy

	• Central Cloudy Dystrophy of François • Pre-Descemet's membrane corneal dystrophy
Cotton (deposits with irregular shape, sheet-like, haze, pigmentation)	**Epithelial and sub-epithelial:** • Thygeson epithelial keratitis • Bacterial keratitis **Bowman layer:** • Thiel-Behnke dystrophy **Stromal:** • Granular dystrophy • Posterior amorphous corneal dystrophy • Corneal amyloidosis **Descemet's membrane and Endothelial:** • Fuchs' endothelial dystrophy • Brown-McLean syndrome
Irregular polygonal	**Epithelial and sub-epithelial:** • Salzmann's nodular degeneration • Gelatinous drop-like dystrophy **Descemet's membrane and Endothelial:** • Iridocorneal endothelial syndrome