DISCUSSION

Ultrasound biomicroscopy is an imaging technology that uses high-frequency ultrasound and thus allows visualization of the anterior portion of the globe in microscopic resolution.

Ultrasound biomicroscopy (DICON P45 UBM Plus) has a 50 MHz transducer. This allows resolution of structures up to 50 microns. It is independent on the clarity of the optical media and allows, for the first time, a non-invasive demonstration of the structures of the anterior segment and their relationship to each other. Therefore, it is especially suitable for diagnosis and research on the various forms of glaucoma (Munnich et al, 1995).

Considering that scarring at the surgical site is the commonest cause of failure of trabeculectomy, the high failure rate in primary cases may be explained in part by the fibrotic conjunctival changes induced by trachoma, or by the fact that many surgeons put their patients on medical therapy for long time and try to avoid surgery as much as they can, and it is well known that topical glaucoma medications decrease the success rate of later glaucoma surgery (Wilkins et al., 2003).

The use of antimetabolite as Mitomycin C as adjunctive treatment with trabeculectomy even in primary surgery is considered to improve the success rate by suppressing the scarring procedure. Effects of MMC include inhibition of fibroblast migration, collagen synthesis. Effects on the vasculature of the conjunctiva and episclera by its vasoconstriction effect vascular endothelial toxicity also could explain its capability to promote filtration surgery success (Jampel, 1992). Intra-operative
Mitomycin C reduces the risk of surgical failure in eyes that have undergone no previous surgery \textit{\textcolor{red}{(Wilkins et al, 2003).}}

Ultrasound biomicroscopy is used to study the functional anatomy of the filtering bleb using high frequency (50 MHz) probe, which provides high-resolution images of filtering blebs. It was possible to obtain longitudinal or transverse images of filtering blebs, to measure the height, to evaluate the reflectivity inside and to follow the route under the scleral flap, so a correlation between bleb shape and intraocular pressure could be evaluated in glaucomatous patients treated with trabeculectomy \textit{\textcolor{red}{(Avitabile et al, 1998).}}

The evaluation of the functional and anatomical characteristics of the filtering blebs recorded the following:
(1) Intraocular pressure and use of any antiglaucoma medications.
(2) Bleb morphology.
(3) Ultrasound biomicroscopic characteristics of the filtering blebs.

- **As regard intraocular pressure:**

  From the statistics, the mean and standard pre-operative IOP of group A were \(28.1 \pm 7.9\) with 50\% of patients were on anti glaucomatous drugs that decreased to 44\% post operative and for group B \(27.1 \pm 5.1\) with 60\% of patients on anti glaucomatous drugs that decreased to 26.7\% post operative.

  The mean and the standard post-operative IOP for group(A) were \(18.5 \pm 4.3 \text{ mmHg}\) and for group (B) were \(13.3 \pm 3.4\). So the mean and the standard deviation of the post-operative IOP of both groups were found to be significantly lower in group (B) than group (A) \((p = 0.001)\). It is considered statistically highly significant.
Regarding success, as group (B) are the cases performed with mitomycin, so the mitomycin has a role in promoting more reduction of the IOP in its cases in comparison to those performed without mitomycin. In group B the percentage of the cases classified as complete success (pure success rate) is 73.3% while in group A the percentage of the cases classified as complete success (pure success rate) is 33.3% which is statistically significant (p < 0.05).

In a study performed by Singh et al., in 1993 to evaluate the efficacy of intra operative mitomycin C in complicated glaucoma upon 10 eyes. The intraocular pressure was successfully controlled in all the ten eyes. The pre operative pressure ranged from 28 to 50 mmHg while the post operative pressure ranged from 7 to 16 mmHg. The intra ocular pressure was successfully controlled in all the 10 eyes and none of the cases required any form of local or systemic medication.

Also in a similar study performed by Wilkins et al in 2003 to evaluate the efficacy and safety of primary trabeculectomy with mitomycin c in reducing IOP in comparison to control cases where primary trabeculectomy had been performed without mitomycin. It was found that the mean postoperative IOP is significantly reduced in group receiving mitomycin c (15.9 ± 4.2 mmHg) compared to placebo (18.2 ± 4.5 mmHg).

Also in a similar study performed by Tsai et al in 2003, the IOP was found to be lower among the group when trabeculectomy done with mitomycin in comparison to the control group performed without mitomycin (10.8±3 mmHg) versus (13.3±3.8mmHg), P< 0.017.
In a similar study performed by *El-Basty et al in 2004*, it was found that the mean and the standard deviation in IOP in MMC treated eyes was (15.28 ± 7.4 mmHg) in comparison to the control group without mitomycin (18.36 ± 7.5 mmHg).

A study with long term follow up to 9 years compared MMC augmented trabeculectomy with non-augmented trabeculectomy. They found that 73.1% of MMC augmented trabeculectomies resulted in IOP less than 18 mmHg without medication compared with 51.1% in the non-augmented group; however, the differences were negligible between the two groups at 3-year follow up (*Relbaldl et al., 2008*).

*Capistrano et al., (2008)* found in their study that the success ratio was 79% in the MMC group of the study.

A study performed by *Lusthaus et al., in 2010* to examine the rates of intermediate-term intraocular pressure (IOP) control after trabeculectomy with mitomycin C on sixty eyes with 3 year follow up. The mean preoperative IOP was 25.33 mmHg (range 8–45 mmHg), with glaucoma medications used in 51 eyes (85.0%). Mean postoperative IOP was 14.0 mmHg (3–31 mmHg, P < 0.001) at 1 year, 14.0 mmHg (4–30 mmHg, P < 0.001) at 2 years and 14.7 mmHg (8–45 mmHg, P < 0.001) at 3 years. Twenty-eight eyes (47%) remained on antihypertensive glaucoma medications at 1 year and 30 eyes (63%) at 3 years. Absolute success rates for criteria 1 (which was measured as IOP less than or equal to 18 mmHg and greater than or equal to 6 mmHg), and criteria 2 (where there had been a 20% reduction in IOP from baseline following trabeculectomy) were 33% at 3 years and qualified success rates at this time were 83% and 79% for criteria 1 and 2, respectively.
Discussion

A study performed by Nilforushan et al., in 2011 in thirty six eyes from 34 patients with uncontrolled glaucoma to evaluate mitomycin C outcomes as adjunctive to trabeculectomy. The mean preoperative IOP in the MMC group improved from 23.3 ± 4.9 mmHg with 2.6± 0.7 antiglaucoma medications to 9.6 ± 2.7 mm Hg with no antiglaucoma medications at the final visit.

- **Bleb morphology**

  In cases performed with miomycin (66.7%) of the blebs tend to be morphologically of type 1 and (33.3%) of type 2 while (53.3%) of blebs performed without mitomycin tend to be morphologically of type 3, (26.7%) of type 2, (13.3%) of encapsulated type and (6.7%) of type 1 bleb.

  In the previously mentioned study by Singh et al., 1993, the all blebs (of the ten eyes) were thin and avascular, showing good filleration.

  *El-Basty et al., in 2004* found that most of the blebs with miomycin tend o be morphologicly with type 1 with infrequent cases of type 2 blebs, while blebs performed without mitomycin tend to be morphologically more with type 3 with infrequent eases of type 2 and encapsulated bleb.

  In the previously mentioned study by Lusthaus et al., in 2010, it was found that at 1 year follow-up, there were 57 patients (95%) of patients had type 1 bleb (diffuse and elevated), 3 patients (5%) had type 2 bleb (cystic), no patients had neither type 3 (avascular) nor encapsulated type. At second year follow-up there were 58 patients (96.7%) had type 1 bleb, 2 patients (3.0%) had type 2 bleb and no patients developed type 3 or encapsulated type. At the third year follow-
up, there were 43 patients (89.0%) had type 1 bleb, 3 patients (5%) had type 2 bleb, 1 patient (1.6%) had type 3 bleb and 1 patient (1.6%) had encapsulated type.

In the previously mentioned study by Nilforushan et al., in 2011, the blebs in the mitomycin group had low to moderate height, a horizontal extension of 2 hours, and mild to moderate vascularization.

- **Ultrasound biomicroscopic characteristics of the filtering blebs:**

  UBM is a very important diagnostic tool for the evaluation of the functional and anatomical characteristics of the filtering blebs. Height, breadth and reflectivity within the bleb could be evaluated using the UBM. Also the aqueous drainage route could be visualized and measured beneath the scleral flap (Yamamoto et al 1995).

  In our study, the **reflectivity of the bleb** was classified according to its similarity to the scleral reflectivity of the same ultrasound biomicroscopic image. The image was classified as having **high** reflectivity when the reflectivity of a particular image was isoechoic or hyper echoic compared with that of the sclera demonstrated in the same ultrasound biomicroscopic image; **low** reflectivity when it was isoechoic compared with that in the standard intrableb image and **medium** reflectivity when it was found to lie between the reflectivities of the standard image and the sclera.

  From the statistics, about 33.3% of blebs of group A and only 6.7% of group B had **high** reflectivity, which were statistically significant (P < 0.05) and about 53.3% of blebs in group A, about 33.3% of group B had **medium** reflectivity which were statistically significant (P < 0.05). Also
about 13.3% of group A and 60% of group B had low reflectivity which were is statistically significant (P < 0.05).

A statistical correlation between the intraocular pressure of the two groups and the reflectivity within the blebs of the two groups shows positive linear relationship, the lower the IOP the lower the reflectivity of the bleb and also the higher the IOP the higher the reflectivity of the filtering blebs. This could explain the presence of low reflectivity within the blebs of mitomycin in association with lower IOP in comparison to the other group with the high reflectivity within the blebs in association with higher IOP. As seen in fig. (45) and (47).

The effect of mitomycin in influencing the internal structure of the blebs could explain the low reflectivity of its blebs due its role in inhibition of fibroblast migration and collagen synthesis reducing the amount of the fibrous tissue within the bleb which is responsible for the high reflectivity within the blebs of the control group. The free spaces within the filtering blebs of mitomycin allow for free percolation of the aqueous which gives the blebs of mitomycin its low reflectivity pattern (Okada et al., 2009).

A similar study performed by Yamamoto et al in 1995 had found that the ultrasound biomicroscopic images of mitomycin blebs with poor IOP control are characterized by high reflectivity inside the blebs.

A study performed by Avitablie et al., 1998, on 46 filtering blebs of 46 patients after trabeculectomy. The UBM examination revealed that blebs with lower IOP had lower reflectivity.

A study performed by Zhang et al., in 2008 that applied upon 69 patients who underwent trabeculectomy to evaluate subconjunctival bleb
function by UBM. There were 17 (24.6%) type L blebs, 19 (27.5%) type H blebs, 4 (5.8%) type E blebs and 29 (42%) type F blebs. Using the standard of Singh et al., of 17 L blebs, 15 blebs were successful, and 2 blebs are non-functioning. Of 19 type H blebs, 15 blebs were successful and 4 blebs were non-functioning. Of 4 type E blebs, 2 blebs were successful and 2 blebs were non-functioning. Of 29 type F blebs, 13 blebs were successful and 16 blebs were non-functioning.

In a study performed by Bello et al., in 2010, to evaluate by ultrasound biomicroscopy (UBM) the filtering blebs and the outcome of trabeculectomy performed with two different concentrations of mitomycin C (MMC) upon 46 eyes from 46 patients. It was found that, intrableb reflectivities and intraocular pressures (IOPs) were lower in the group received 0.4 mg MMC than that of the group received 0.2mg MMC.

The height of the bleb was measured as the length of the longest line from the surface of the sclera to that of the bleb, measured perpendicular to the sclera.

From the statistics, the mean and the standard deviation of the height of the bleb for group (B) was (1.126± 0.611 mm) while the group (A) is (0.353 ± 0.227 mm). So the mean and the standard deviation of the height of both groups are found to be significantly higher in group (B) than group (A) (p < 0.01), which was considered highly significant.

It was found that The height of one case (8.33%) of group (A) and 13 cases (86.66%) of group (B) ranging between (> 1 mm - > 0.5mm). and 11 cases (91.66%) of group (A), 2 cases (13.33%) of group (B) were (< 0.5 mm).
A statistical correlation between the intraocular pressure of the two groups and the height of the blebs of the two groups shows inversed relationship, the lower the IOP the higher the height of the bleb.

This could explain the presence of high blebs of mitomycin with lower IOP in comparison to the other group with lower blebs and higher IOP. As seen in fig. (49), (50).

A study performed by Yamamoto et al in 1995 using UBM for the evaluation of the heights of the mitomycin blebs only. It had been found that blebs of mitomycin tend to be high blebs (number of blebs above 2 mm in height in comparison to the total number of the mitomycin blebs is 46 to 89 respectively, percentage is 51 %, P< 0.0001).

In the previously mentioned study by Avitabile et al., 1998, it was found that the blebs with lower reflectivity and a visible route under the scleral flap had a lower intraocular pressure while the height was not important for a good intraocular pressure.

A similar study performed by El. Basty et al., in 2004 the mean and standard deviation of the height of the bleb for mitomycin group was (1.811 ± 0.52mm) in comparison to control group which was (1.325 ± 0.40mm) so the mean and the standard deviation of the height of both groups are found to be significantly higher in mitomycin group than control group (p < 0.00064). It was considered statistically highly significant.

In the previously mentioned study by Bello et al., in 2010, it was found that filtering blebs were higher, in the group receiving 0.4mg MMC than the other group.
The transverse diameter of the bleb (breadth) is defined as the longest line, which is perpendicular to that which is used of measurement of the bleb height. This line connects a point, which is the beginning of the conjunctival bleb at the corneal side to a point where the conjunctival bleb ends at the scleral side.

From the statistics, the mean and the standard deviation of the breadth of the blebs for group (A) was \((1.771 \pm 0.553 \text{ mm})\) and for group (B) was \((2.472 \pm 0.618 \text{ mm})\). So the mean and the standard deviation of the breadth of both groups are found to be significantly higher in group (B) than group (A) \((p = 0.01)\), which was considered statistically highly significant.

It was found that the breadth of 4 cases (33.3%) of group (A) and 11 cases (73.33%) of group (B) was \(> 2 \text{ mm}\) and 8 cases (66.7%) of group A and 4 cases (26.6%) of group B was \(< 2 \text{ mm}\). see.

A statistical correlation between the intraocular pressure of the two groups and the breadth of the blebs of the two groups shows inversed relationship, the lower the IOP the higher the breadth of the bleb. This could explain the presence of higher values of the breadth of the blebs of mitomycin with lower IOP in comparison to the other group with lower values of the breadth of the blebs and higher IOP.

So the blebs of mitomycin have higher values of the breadth than the blebs of classic trabeculectomy as proven by UBM and this is associated with more efficient control of the IOP in those cases. See table (35), (36).

A similar study performed by *El- Basty et al., in 2004* the mean and the standard deviation of the breadth of the blebs for control group
was (4.1825 ± 0.483mm) and for mitomycin group was (4.4998 ± 0.488mm). So the mean and the standard deviation of the breadth of both groups are found to be significantly higher in mitomycin group than the control group (P <0.04), which was considered statistically significant.

The ultrasound biomicroscopic images were evaluated for the visibility of the aqueous drainage route. If the route could be identified and followed along the entire scleral flap, the route was classified as visible and measured, if it couldn't be identified and followed along the entire scleral flap it was classified as non or poorly visible.

From the statistics, the mean and the standard deviation of the aqueous drainage route measurement for group (A) was (0.726 ± 0.257 mm) and for group (B) was (0.782 ± 0.326 mm). So the mean and the standard deviation of the aqueous drainage route measurement of both groups are found to have not enough statistically significant difference in group (B) in relation to group (A), (p >0.05).

But as regard route visibility, 20% of group A was poorly visible whereas no. poorly visible routes detected group B.

It was found that the aqueous drainage route of 10 cases (83.33%) of group (A) and 11 cases (73.33%) of group (B) ranging between (> 1m - > 0.5 mm) and 2 cases (16.66%) of group (A) and 4 cases (26.6%) of group (B) was (< 0.5 mm).

A statistical correlation between the intraocular pressure of the two groups and the visibility and measurement of the aqueous drainage route within the blebs of the two groups shows inverse relationship. The lower the IOP the more visible the aqueous drainage route and also the higher
the IOP the less visible the aqueous drainage route of the filtering blebs see table (35), (36).

A similar study performed by Yamamoto et al 1995 had found that the ultrasound biomicroscopic images of mitomycin blebs associated with poor IOP control are characterized by lesser visibility of the aqueous drainage route under the scleral flap and higher reflectivity inside the bleb.

In the previously mentioned study by Avitabile et al., 1998, the UBM examination revealed that blebs with lower intraocular pressure had a more visible route under the scleral flap.

In a study performed by Jinza et al., in 2000, upon eyes of 21 patients, it was found that development of a filtering bleb was correlated with the efficiency of filtration beneath the scleral flap in eyes that had undergone trabeculectomy.

El-basty et al., in 2004, found inverse relationship between IOP and measurement of the aqueous drainage route within the blebs. The lower the IOP the more visible the aqueous drainage route and also the higher the IOP the less visible the aqueous drainage route of the filtering blebs.

Regarding post operative complications, the early post operative complications were minimal including mild conjunctival chemosis, mild anterior uveitis, mild AC shallowing that resolved with local pressure bandage. One eye of group (B) showing hypotony (IOP less than or equal to 6mmHg) where no cases were found in group (A). Hypotony maculopathy was found in that case with decrease in visual acuity in such case.
The most frequent late complication was cataract which developed in 9 cases (60%) in group (B) performed with mitomycin in comparison to group (A) 5 cases (33.3%) at 6 months follow-up.

**Kitazawa and His group in 1993**, showed (18%) incidence of cataract in MMC eyes after one year follow up, **Beckers et al., in 2003**, followed up patients after trabeculectomy with mitomycin for two years, they found that cataract had developed in thirteen eyes out of a total of sixty eyes (22%). The high incidence of catraract may be explained by the fact that the decrease in IOP in MMC eyes was too much when compared to precoperative value, a condition which might had interfred with lens metabolism (**Beckers et al., in 2003**).

**Tsai et al. in 2003**, found that hypotony maculopathy occurs more frequent among mitomycin group in comparison to control group (20 versus 0% respectively).

**El-Basty et al., in 2004**, showed an incidence of 8 cases of cataract (26.6%) in comparison to control group 2 cases (6.6%).

In the study performed by **Giampani et al., in 2008**, the post operative complications were : a flat anterior chamber in five eyes (3.04%), hyphema in two eyes (1.21%), bleb leak in one eye (0.6%) and endophthalmitis in eight eyes (4.88%).

The delayed complications of **Lusthaus et al., in 2010**, were one cases of cataract (1.6%) and one shallow anterior chamber (1.6%) at 1-year follow up.

The study of **Nilforushan et al., in 2011**, reported one eye (5.5%) in the MMC group required choroidal drainage and anterior chamber formation because of persistant choroidal detachment 3 months after surgery.